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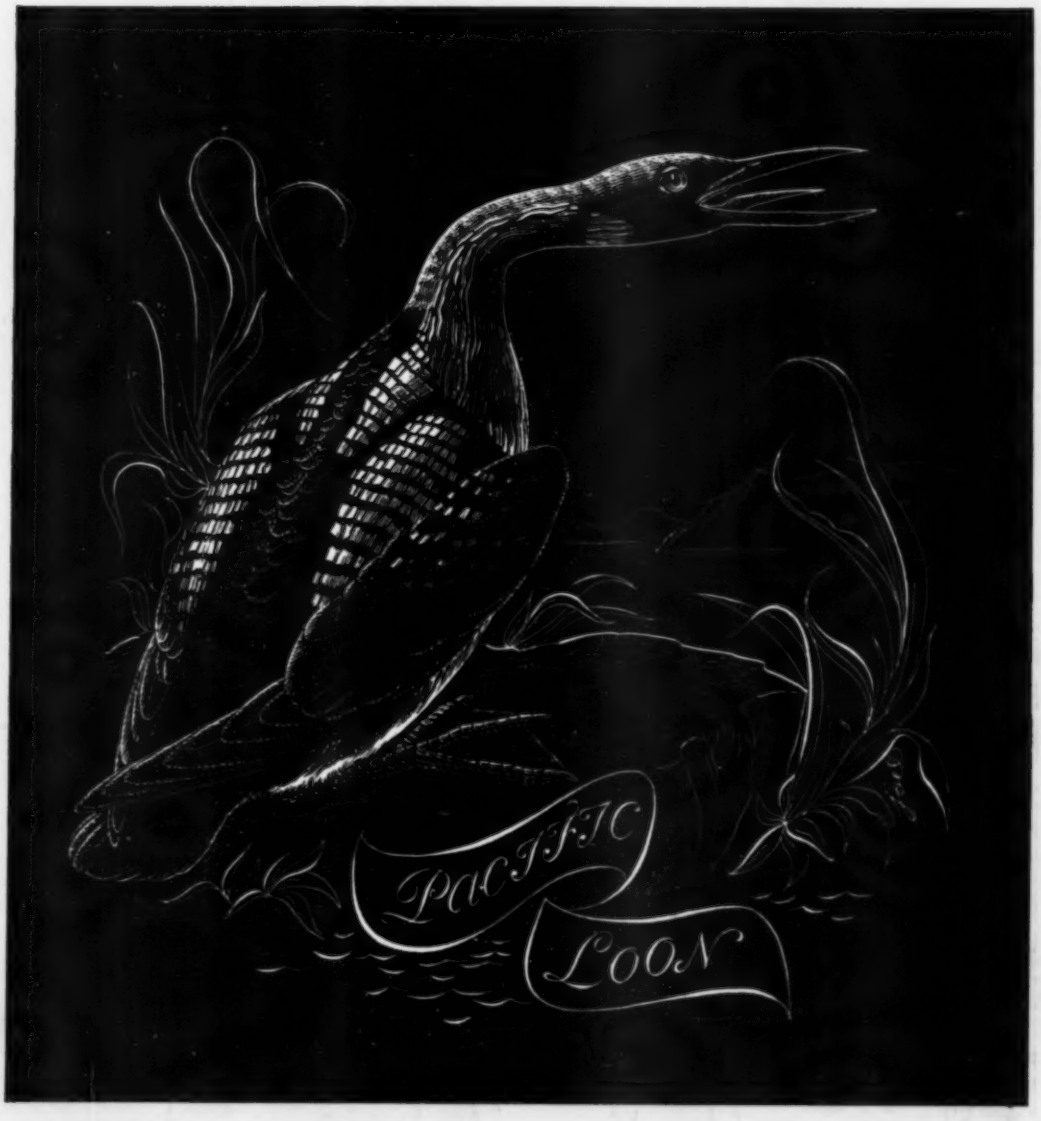
July 1956

Drug and Cosmetic Industry



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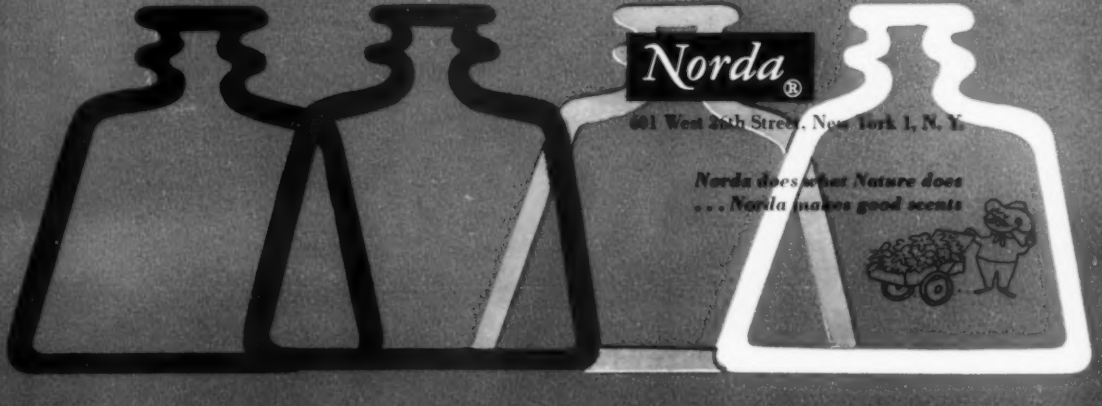

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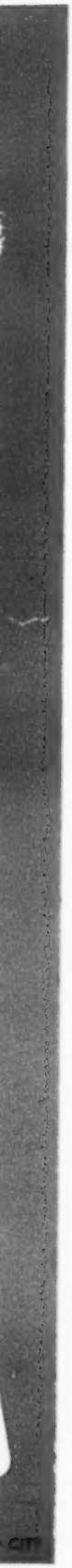
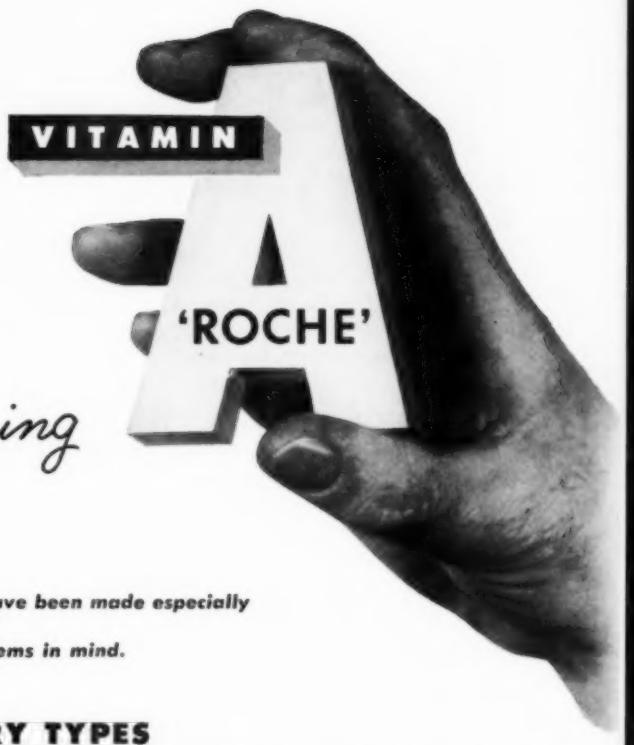


Memo to: executives, purchasing agents, technical people

Roche has all popular types of Vitamin A for your pharmaceutical manufacturing



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pe A1MO vitamin A acetate—1,000,000 U.S.P. units per gram, stand-dized by addition of edible oil. Contains well-proven stabilizing factors the Roche synthesis.

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se special types are available for research and special production in ch special handling can be provided.

•

kaging—All liquid types of 'Roche' vitamin A are packed under inert in seamless containers. Nominal quantities are shipped in wide-th aluminum bottles. For large orders, a specially-designed alumi-transport can holding 50 kilos is recommended. A dispensing attach-t is available.

ples on request; ask your Roche salesman or write Vitamin Division.

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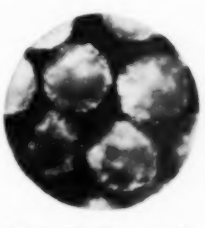
'Roche' dry vitamin A acetate, and vitamin A and D_3, powders have grea advantages.



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Second, having an irregular surface the Roch product does not separate from other dry ingre dients during mixing or vibrating.

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Fourth, dry vitamin A acetate 'Roche' has high stability in tablets, hard and soft gelatin capsules and powdered food supplements.

The following Roche types have been found most popular:

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Packaging. All types of 'Roche' dry vitamin A are packed in polyethylene bags, with protective sealer, in drums and in 1 and 2 kilo tamperpruf metal con-tainers. Small quantities in amber screw-cap bottles.

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"The boss is sore as nett that we never came up with anything to cure ileitus without surgery."

Keeping Posted

A.D.M.A.-A.P.M.A. Merger Proposed

The idea of bringing together into one association of pharmaceutical manufacturers the members of the American Drug Manufacturers Association and the members of the American Pharmaceutical Manufacturers Association has been under definite consideration for about two months. The idea of such a merger has been mentioned for more years than we care to think about, because as long ago as twenty-five or thirty years, these two associations had a common membership of about fifty per cent. The main difference in membership at that time was that the American Drug Manufacturers Association had all the large manufacturers and relatively few of the small ones, while the American Pharmaceutical Manufacturers Association had relatively few of the large manufacturers, and many small ones.

Today the situation as regards the large manufacturers is that they are all members of both associations with two notable exceptions. These exceptions are Eli Lilly and Company and The Upjohn Company which are still members only of the American Drug Manufacturers Association.

The numerous other associations for special purposes which have been organized in recent years, and which are supported solely, or almost solely by the pharmaceutical manufacturers is steadily increasing the burden to be carried by these companies both in time and money. Some of these are the Health Information Foundation, the National Pharmaceutical Council, and the recently formed Health News Institute.

Some of the advantages which might accrue from a merger of the A.D.M.A. and the A.P.M.A. are a saving in the amount of dues to be paid, a saving in both time and money due to the fact that there will be no duplication of annual and other meetings, and the fact that the pharmaceutical manufacturing industry will be able to present a united front in the problems which confront the industry.

While probability of merger very definitely exists, it has not as yet been accomplished. The progress made was revealed on June 18 in the following official statement released by Dr. J. O'Neill Closs, executive secretary of the American Pharmaceutical Manufacturers Association:

"At a special meeting of the board of directors of the American Pharmaceutical Manufacturers Association at Chicago on June 12th, it was unanimously voted to explore the possibilities and mechanics of establishing a single new association to represent the pharmaceutical industry.

"Committees representing the American Drug Manufacturers and the American Pharmaceutical Manufacturers Association met jointly the following day to implement the A.P.M.A.'s vote which had been preceded by similar vote in the A.D.M.A. executive committee.

"Spokesmen for the committee emphasized that only exploratory work had been done to date and that many problems would have to be resolved before any final recommendations could be formulated.

"The membership of the committees are as follows: "For the A.P.M.A.: Francis Brown, The Schering Corporation; M. F. Charley, Standard Pharmacal Company; Robert K. Cutter, M.D., Cutter Laboratories; William B. Graham, Baxter Laboratories; Robert A. Hardt, Hoffmann-La Roche, Inc.; Edgar L. Patch, Armour Laboratories; S. B. Penick Jr., S. B. Penick & Company; Jack Schopflin, E. S. Miller & Co.; K. F. Valentine, Pitman-Moore Co.

"For the A.D.M.A.: E. N. Beeseley, Eli Lilly and Company, J. H. Fitzgerald Dunning, Hynson, Westcott & Dunning; Leslie D. Harrop, The Upjohn Company; John G. Searle, G. D. Searle & Co.; Ernest H. Volwiler, Abbott Laboratories; K. F. Valentine, Pitman-Moore Co."

In a statement on the subject, Ernest H. Volwiler, president of the A.D.M.A., said:

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An Aldehyde of great stability and of such high degree of purity that it can be used in the finest perfume extracts as well as soaps and cosmetics.

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An Acetal resembling the aroma of Reseda Mignonette. It is a valuable addition to all floral bouquets, and as a modifier for the purpose of rounding off all types of compositions.

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An Acetal, ideal for all rose type compounds, because of its fine character, great lift and extreme stability.

The advantage of these aromatic chemicals is that their great purity permits their use in the most luxurious perfumes . . . and their low cost makes them feasible for even the most inexpensive soap fragrances.

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"Through the years the two associations have maintained a number of joint or combined activities, beginning with the Combined Pharmaceutical Contact Committee in 1924. Some of the combined groups which have been, or presently are, actively working on behalf of the two associations are the Combined Trade-Mark Bureau, the Joint Committee on New Drug Regulations, the Joint Task force on Antibiotic Certification, the Joint Committee on Trade-Marks, and the Joint Committee on the International Pharmacopoeia. Proposals have been made for a Combined Legislative Committee and a Combined Medical Section.

"Many members of the industry recognize the value of these joint efforts, and believe that they should be extended. They also recognize the difficulty of operating these joint committees, in which each problem of policy must be referred back to two independent governing bodies, differences reconciled, and then studied again. Furthermore, the comment is frequently made that the industry sometimes is difficult to present a united front on legislative and regulatory problems because of organizational complexities. It has been pointed out that a single association could intensify the good features of both groups, and eliminate duplication."

Dr. Volwiler pointed out that A.D.M.A. Executive Committee and the A.P.M.A. Board of Directors will meet in the Fall, and at that time will receive their committee reports. Furthermore the A.D.M.A. Executive Committee will refer any definite proposal to the association membership for study and consideration.

Warner-Chilcott Scholarships

As one way of observing Warner-Chilcott Laboratories' one hundredth anniversary, the company has announced a type of scholarship unique in the pharmaceutical industry. Four two thousand dollar awards will be made annually to high school graduates for four years study in one or more of the natural sciences. Students are not restricted to any individual science but can select from any of the broad field of natural sciences.

"We decided on this type of scholarship," said Warner-Chilcott vice-president E. R. Beckwith, "because we believe it is the best way to help meet the great need for scientists in both the nation and our industry. We did not wish to dictate just what a student should be, but rather we wanted to encourage deserving boys and girls to make careers in science."

The first four winners will be selected this year from among the graduates of New Jersey high schools by the Scholarship Sub-committee of the North Jersey Section of the American Chemical Society. The students' grades, special tests, personal interviews, and financial need will be among the factors considered. The two thousand dollars will be paid in annual five-hundred-dollar installments to the college of the student's choice. If a student selects one of nine colleges in Northern New Jersey cooperating with the ACS, the college will add a grant of four hundred dollars to the Warner-Chilcott scholarship.

Doctors and the President

Those members of the medical profession serving President Eisenhower in his recent illness certainly acted strangely as compared with the physicians which the ordinary individual runs up against. From our viewpoint they do not appear to be performing any good for the medical profession as a whole, for the public, or for themselves. The idea of announcing within a relatively few hours after major surgery was performed that the patient will definitely be well enough within about six weeks to take on a full load of work in what is probably the most back-breaking job in the world, must sound very strange to those people who have talked to the cagey average doctor who never can be sure because in the great store of his medical knowledge he knows that so many things can happen—and often do—to upset any certain prediction that he might make. Even pharmaceutical manufacturers have learned to be cautious regarding their new drugs because they, like the doctors, have become strongly aware of the uncertainties that are present in treatment with any type of therapy.

One can anticipate that the average doctor is going to be faced by irate relatives for certain answers in all sorts of cases. And if the doctor continues to equivocate, he is going to be considered not as qualified as the doctors who treated President Eisenhower, and in many cases he is going to be told so.

McKesson and Fair Trade

The U. S. Supreme Court, by a split decision, ruled against McKesson & Robbins in its attempt to fix prices at wholesale under the Miller-Tydings and McGuire fair trade enabling acts. The court ruled that identical fair trade prices may not be set with both independent wholesalers and a producer's subsidiary wholesalers. This, the court maintained, is price fixing, illegal under the Sherman Act where two sets of wholesalers are in competition with each other. The majority opinion found that "Congress made as plain as words can make it that, without regard to categories or label, the crucial inquiry is whether the contracting parties compete with each other. If they do, the Miller-Tydings and McGuire Acts do not permit them to fix resale prices."

The minority opinion protested that "there is no meaningful distinction between the fair trade contracts of integrated and non-integrated manufacturers," saying also, "the necessary result—indeed, the very object—of fair trade laws is to permit the elimination of price competition in the branded products among those who sell it."

This ruling by the U. S. Supreme Court has come as quite a surprise to those who thought that the court would follow its ruling in the Eastman Kodak case. In that case, even though Eastman owned retail stores, it was permitted to maintain fair trade prices of goods of its own manufacture sold at both its own stores and at other retail stores which are competitive with the Eastman stores.

Commenting on the decision, McKesson & Robbins said:

"While the decision of the Supreme Court, invalidating

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fair trade agreements between McKesson & Robbins, Inc. and wholesalers, is disappointing, the Court has spoken and we are taking immediate steps to comply with its ruling. At the same time, we shall continue to support, as we have consistently supported in the past, the principles of fair trade in every lawful manner and in accordance with the view of the Court. It is to be noted that our retail fair trade contracts are in no way questioned."

Pfizer Plant for Italy

A plant to produce antibiotics, other pharmaceutical products, and animal feed supplements is to be built in Italy by Chas. Pfizer & Co. A factory site which will eventually occupy 30 acres has been acquired at Latina, about 40 miles southeast of Rome. Construction is starting this month and operation is anticipated by the Spring of 1957. The new plant will be operated entirely by Italian personnel. Pfizer's scientific and technological knowledge and skills will be combined with Italian technology to provide Italy with the most modern plant possible, according to Pfizer president John E. McKeen.

Pfizer opened plants in England, France, and the Philippines last year, and also has manufacturing facilities in Brazil, Spain, Germany, Belgium, and a number of other countries. Plants will be opened in Canada, Chile, and Japan later this year.

Dr. Schaefer Retiring

Dr. Hugo H. Schaefer, president of the National Drug Trade Conference and dean of Brooklyn College of Pharmacy, is retiring as dean of the pharmacy college September 1, after having served 19 years in that capacity. In recognition of Dr. Schaefer's many contributions to public health, Long Island University conferred on him an honorary degree of Doctor of Laws at the annual commencement on June 8. Dr. Schaefer was the 1951 recipient of the Remington Honor Medal, the highest award of American Pharmacy for constructive achievement.

Change in Cosmetic Seminar Dates

Due to many early requests for reservations for the Third Cosmetic Seminar, the total attendance has been increased to 250. This has necessitated a change in the scheduled dates from September 27 and 28, to October 4 and 5, in order to obtain the auditorium of the Barbizon-Plaza Hotel for the meetings. The two luncheons, cocktail party and dinner will be held at the New York Academy of Sciences.

Schering and Patents

The U. S. Supreme Court has refused to review the decision of the U. S. Court of Appeals which upheld the U. S. District Court decision which ruled that Schering Corporation must issue licenses on its patents issued between 1942 and 1952. Among these patents is one covering Schering's Chlortrimeton. It was this patent that started the fuss.

Helene Curtis Industries

Helene Curtis Industries, Inc., has two divisions, the Toiletries Division and the Beauty Salon Division, according to the prospectus issued in connection with the company's recent sale of 375,000 shares of Class A stock, par value $1, selling price $10.

The Toiletries Division, which sells only products intended for ultimate retail purchase (other than persons buying from beauty salons), distributes through wholesalers and directly to major department stores, drug, chain, and food outlets. The products of this division include: Suave, hairdressing for women in liquid and creme form; Suave for Men, hairdressing in plastic container; Spray Net, believed by Company to be largest selling women's hair fixative in the world—aerosol packaged; Shampoo Plus Egg, shampoo with whole egg added; Lanolin Shampoo, sold in either liquid or creme form; Lanolin Discovery, aerosol packaged preparation for beautifying, conditioning and highlighting hair; Creme Rinse, an after-shampoo rinse.

The Company is test-marketing Enden, a new shampoo for control of dandruff symptoms, and a new purse-size dispenser and refill container for Spray Net has been developed.

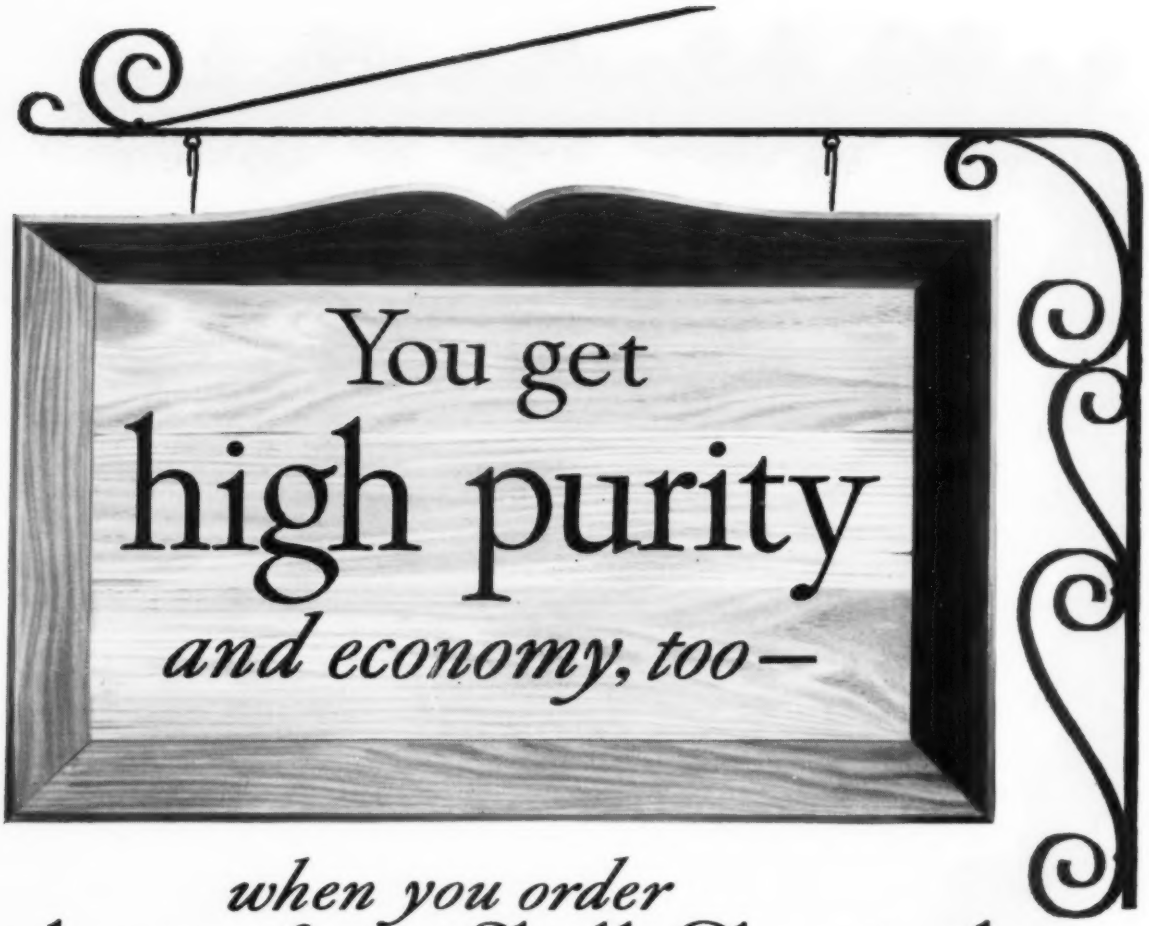
The Toiletries Division, which has concentrated on hair preparations, principally for women, has now acquired rights to men's preparations sold under the trademark Kings Men, the major items being a man's cologne, pre-shave and after-shave lotions, an aerosol dispensed shaving cream and a deodorant. Also the Toiletries Division is marketing Stopette and affiliated products.

The Beauty Salon Division sells a complete line of permanent wave solutions distributed exclusively to professional beauticians under various trademarks, the best known of which are Heavenly, Rhapsody, and Fashionwave. The division also sells a complete line of additional products and equipment used by professional beauticians for the care of the hair, including permanent hair waving machines, hair dryers, curlers, spacers, and clips. In 1955, the Company introduced a new type hair dryer. Many of the products of the Toiletries Division are also used in beauty salons and are sold through them to their patrons for home use. Sales of this division are effected through authorized dealers, and sales are made directly to certain chains of beauty salons.

In 1955, percentages of sales by products groups were: Aerosol Dispensed Products (Spray Net and Lanolin Discovery), 46 per cent; Shampoo and Permanent Wave Solutions, 33 per cent; Suave and Creme Rinse, 16 per cent; all other, including beauty salon equipment, five per cent. The proportion of gross profit attributable to each of these groups did not vary more than four per cent from its proportion of total sales.

Of total sales by the Toiletries Division in 1955, 48 per cent were to drug wholesalers, chains and retailers; 37 per cent were to food wholesalers, chains and retailers; eight per cent were to variety stores; and seven per cent to department stores and others.

In 1955 the Toiletries Division accounted for 64 per cent of total sales and 72 per cent of the operating



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- Diacetone Alcohol
- Secondary Butyl Alcohol
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profit. The Beauty Salon Division accounted for 36 per cent of total sales, and 28 per cent of operating profit.

Sales for 1955 totaled $29,700,959, against $25,131,228 for 1954, $18,801,931 for 1953, $14,988,702 for 1952, and $10,633,231 for 1951. Toiletries Division sales were: 1955, $19,053,143; 1954, $14,819,653; 1953, $8,761,683; 1952, $5,206,721; and 1951, $2,716,772. Beauty Salon Division sales were: 1955, $10,526,736; 1954, $10,175,446; 1953, $8,996,506; 1952, $8,426,055; 1951, $7,547,051. Sales of other divisions, in which are included defense production sales for 1951, 1952, and 1953, of $317,013, $1,319,705, and $1,007,108, respectively, were: 1955, $121,080; 1954, $136,129; 1953, $1,043,742; 1952, $1,355,923; and 1951, $369,108.

Net earnings of the Company were: 1955, $1,738,425; 1954, $1,170,149; 1953, $302,283; 1952, $72,980; and 1951, $204,392.

Advertising expenditures were: 1955, $7,874,808; 1954, $6,247,808; 1953, $3,612,326; 1952, $2,686,990; 1951, $1,382,805.

The Company's capitalization consists of a loan of $260,000; 50,832 shares of 50 cents Cumulative Sinking Fund Preferred Shares, $5 par, 900,000 shares Class A stock, and 600,000 shares Class B stock, $1 par.

Trading Stamps Impede Fair Trade

A Massachusetts judge refused to issue a preliminary injunction to Colgate-Palmolive Company against certain retailers charged with fair trade price violations because Colgate had acquiesced to, and tolerated the use of trading stamps in connection with the sale of their products at retail. However, the court intimated that if this practice was eliminated, the case might be brought before the court again.

Pharmaceutical Advertising

Pharmaceutical product advertising in medical journals and by direct mail cost advertisers just over $19 million for the six months ended March 31, 1956, according to Medical Promotion Records, Inc. Allowing for the anticipated seasonal decline during the Summer, this would indicate a twelve-month expenditure of about $36 million—considerably less than industry "guesses" in the past. The studies revealed that during the six-month period the business was almost evenly divided between the medical journals, which accounted for $9,552,000, and direct mail at $9,503,000. The journal advertising figure is based on an ad-by-ad and issue-issue tabulation of all pharmaceutical product advertising in the 180 national, sectional, and state journals plus 80 of the largest city and county bulletins. The direct mail figure is arrived at by developing mailing patterns through the tabulation of the mail received by 74 doctors of various types and locations. The dollar values quoted include charges for space, color, position, and bleed in the case of journal advertisements. The direct mail dollar values include estimated costs for printing, inserting, addressing, mailing, and postage. Thus the dollar values do not include the cost of advertising research, copywriting, or artwork.

Each of eight companies spent over $600,000 during the six months indicating an annual expenditure of over a million dollars each. The advertisers spent over $200,000 during the six months on each of five brands or specialties.

Medical Promotion Records comments: "The interest in these figures lies in the fact that they are so low compared with accepted levels of expenditure on consumer products. The figures do not, of course, include the cost of detailing."

Harry J. Knox, president of the organization, says a measurement of detailing is the next project to be tackled.

Raw Material from Shrimps

A new raw material for this industry, as well as for others, is being obtained from shrimp shells. Deacetylated chitin is produced from chitin which exists in various forms in crabs, lobsters, shrimp and crayfish, as well as grasshoppers, various forms of fungi and hard-shell beetles. Kylan Corporation is obtaining chitin from shrimp shells readily available in the area adjacent to Brunswick, Ga. It is said that when using this raw material as an emulsifying agent and protective colloid, it is possible to prepare pharmaceutical and cosmetics emulsions having pH's approximating the pH of the skin.

U.S. Reserpine Patent to Ciba

Ciba, the company which first isolated and introduced reserpine, is now the holder of U. S. Patent No. 2,752,351, which was issued on June 26 to Dr. Emil Schlittler, vice-president and director of research at Ciba Pharmaceutical Products Inc., and Dr. Johannes Mueller, research chemist at the parent company, Ciba Limited of Basle, Switzerland, who assigned the patent to Ciba. The patent contains eight claims embracing crystalline reserpine, its salts and pharmaceutical preparations of the drug. Ciba and its affiliates hold patents on reserpine in many other countries of the world.

Introduced by Ciba in 1953 under the brand name Serpasil, the drug accounted for about $14 million in sales for Ciba Pharmaceutical Products Inc. during 1955. The entire United States reserpine market last year is estimated by Ciba at $25 million.

The work on the investigation of rawolfia serpentina was started in the Ciba Laboratories, Basle, Switzerland, in 1946 by Dr. Schlittler and Dr. Mueller. In September of 1952 together with Dr. Hugo J. Bein, a Ciba Limited pharmacologist, they reported their findings. They had succeeded in isolating and identifying a pure crystalline alkaloid from the rawolfia serpentina that would produce the sedative and hypotensive effect of the whole root which had been known for centuries in India as a tranquilizing agent employed in the treatment of a multitude of illnesses ranging from anxiety to high blood pressure.

Receives Library Award

Irene M. Strieby, library consultant at Eli Lilly and Company, has received the 1956 Professional Award of the Special Libraries Association.

Fluoridation Promotion

The Committee to Protect Our Children's Teeth, Inc., was formed last month to spread facts and correct misinformation on fluoridation of water supplies. The committee's chairman, Dr. Benjamin Spock, said the campaign will concentrate on New York City where the Board of Health has recommended the measure repeatedly. He said that "persons in many parts of the country are joining the committee because New York's decision will be pivotal and perhaps decisive in advancing the measure across the country." He called fluoridation "the safest, most effective, and cheapest way to protect children's teeth" and added that "up to ten years of successful use of the procedure by more than 1,100 communities across our country have proved its efficiency and absolute safety."

Dr. Spock, visiting professor of child development at Western Reserve University, Cleveland, is author of many books on child care.

The State Charities Aid Association, voluntary organization which is cooperating with the committee in its educational campaign, is accepting contributions toward a $100,000 budget for "an intensive campaign through all available media," said Dr. Spock.

In literature accompanying invitations to membership on the committee, Dr. Spock says that "findings show that children's dental decay is reduced as much as 60 to 65 per cent by proper fluoride addition to water supplies." He said the procedure is now in use in 24 of America's largest cities, including Chicago, Philadelphia, Milwaukee, Baltimore, Cleveland, St. Louis, and Washington, D. C.

Animal Research Center

A center for research on feed additives and drugs for poultry, farm animals and household pets has been established by Abbott Laboratories on a 207 acre Lake County farm 17 miles southwest of Abbott's North Chicago plant. Dr. Ernest H. Volwiler, Abbott president, explains:

"The projected farm research center is expected to implement the development of research data necessary to sustain and stimulate the company's expanding agricultural and veterinary program. The nutrition, care and treatment of animals today is an extremely challenging area of research. Because of nutritional deficiencies and disease, one in ten chickens, turkeys, and meat animals do not live to go to market. Since American farmers have an investment of some $28 billion in livestock, the annual economic toll from disease is a staggering $2.8 billion."

Warner-Lambert in England

Warner-Lambert Pharmaceutical Company opened a new $1.5 million manufacturing plant in Eastleigh, England, last month. The ultra-modern plant comprises 104,000 square feet on a 16-acre site near Southampton. It will manufacture $5 million worth of pharmaceuticals and cosmetics annually for distribution in the United Kingdom.

Shulton Pharmaceuticals

Shulton, Inc. has formed a new Pharmaceutical Division to market a "quality line of proprietary pharmaceuticals." The first items are Thylox Medicated Soap and Thylox Medicated Cream, "clinically tested products for the treatment of acne and other skin conditions." Additional products being developed by Shulton research will expand this new line of "medicated skin and scalp pharmaceuticals." Roy Stagner is manager of the new division.

Takes 13 Commencement Awards

Scanning the printed program of the 135th commencement of the Philadelphia College of Pharmacy and Science, we were quite overcome with the accomplishments of one Stella Kamradziuss. This lady, with three other students was designated as "Distinguished" with a general average of 90 per cent or over. She was awarded a gold medal from the Alumni Association for the Bachelor of Science in Pharmacy student who attained the highest scholastic average over the four years. She was awarded the Procter Prize—a gold medal awarded to the Bachelor of Science in Pharmacy student having the highest average in the senior year. She received the Josiah C. and Bertha L. DeG. Peacock Proficiency Prize of two hundred dollars offered to the winner of the Procter Prize. She also received the Remington Memorial Prize of twenty dollars awarded to the Bachelor of Science in Pharmacy student with the highest average in Operative Pharmacy and Dispensing. Next she received the Frank Gibbs Ryan Prize, a gold medal, awarded for the best average in Chemistry and Pharmaceutical Laboratory courses. In addition she received the Mahlon N. Kline Theoretical Pharmacy Prize of fifty dollars for the candidate with the highest average in Theory and Practice in Pharmacy. Also she received the William B. Webb Memorial Prize of twenty-five dollars for the highest average in the branches of Operative Pharmacy, Analytical Chemistry, and Pharmacognosy. Next she received the Frederick William Hausman Memorial Prize of one hundred dollars awarded to the Pharmacy student with the highest average for the last three years. Then she received the Philadelphia Association of Retail Druggists Ladies' Auxiliary Prize, an engraved mortar and pestle, awarded to an outstanding woman student in Pharmacy on the basis of scholastic achievement. The next she received was the Anslinger Award, bound copies of the History of Pharmacy by Kramers and Urdang and The Narcotic Drug Traffic by Anslinger and Thompkins. Finally she received the Abraham Krigstein Memorial Award, membership in the American Pharmaceutical Association, given to the major in Pharmacy with the highest average in Theoretical and Professional Pharmacy. In addition she was one of the four winners of the Merck Awards, consisting of the current Merck publications, presented to the two Pharmacy seniors who have attained the highest standing in Operative Pharmacy and in Theoretical Pharmacy in the last two years of the course, and to the two chemistry seniors who have attained the highest standing in the chemistry course.

JOHN G. SEARLE

G. D. SEARLE & CO.

An inside study of a little-known but truly extraordinary management is the description which The American Institute of Management gives to its "Management Audit" of G. D. Searle & Co.

"Founded in 1888 by Gideon Daniel Searle," the Audit points out, "the company manufactured a general line of standard formula pharmaceuticals until about 1920, when its dependence upon its own research was initiated. The company's greatest growth has taken place in the last two decades, under the direction of John G. Searle, grandson of the founder. In this period, as the result of a series of policy decisions, the company has limited the drugs it manufactures to those which represent an advance in chemotherapy. In addition, it has concentrated an exemplary research program on an area of greatest fruitfulness: the field of degenerative diseases, those associated with old age.

"Today Searle markets about twenty-five pharmaceuticals. Over 97 per cent of its annual sales ($26 million in 1955) derive from products it has developed in its own laboratories. While Searle produces none of the spectacular antibiotics, sulfa drugs, or vitamins which brought growth to other pharmaceutical companies, it has expanded rapidly as a result of its directed research program. Its success has, in fact, stimulated research throughout the drug industry. . . .

"John G. Searle, president, is the principal executive officer. Reporting to him are three vice-presidents: P. E. Tillman, senior vice-president; F. P. O'Brien, vice-president of sales and distribution; and Dr. A. L. Raymond, vice-president of research and development. These three executives are also members of the board of directors. . . .

"Production quality control, like research, has particular importance in the manufacture of potent drugs. At Searle it is held as important as production itself. The control department reports directly to the president, rather than to the production manager. This procedure, now increasingly common in pharmaceutical companies, was a unique means of assuring absolute product quality when instituted at Searle. . . .

"G. D. Searle & Co. has steadily increased its net income before taxes from $218,000 in 1936 to $13 million in 1955, a 6,000 per cent increase. Net income after taxes has followed the same growth pattern, rising to over $6 million in 1955.

"The significant trade cycles of the past thirty years have, in fact, had little effect on the company. Aside from the year 1932, earnings growth have been more-or-less independent of the general economy. For example, the company operated at new highs of sales and profit during the recessional period of 1949, and while earnings in most of the pharmaceutical industry fluctuated excessively from 1951 to 1954 because of competitive stresses, Searle's remained stable. . . .

"Drug research remains hotly competitive, and the 'useful life' of the average drug product grows shorter. Research results, furthermore, are often unpredictable. Nevertheless, the concentration of one of the finest and largest scientific staffs in the pharmaceutical industry upon a limited field of drug research almost assures Searle of continued product development.

"The present sales organization is already prepared to exploit any new products that the company might develop in the next few years. In addition, Searle's expansion in the foreign drug market should provide further growth in income. . . .

"G. D. Searle & Co. is owned entirely by common stock interests. Until 1950, 93 per cent of this stock was held by members of the Searle family and most of the remaining seven per cent by other directors and officers. In 1950 part of the Searle family's holdings was offered to the public and to employees of the company, reducing the family's interest to 59 per cent. The company now has about 3,500 shareholders. . . .

" 'Research in the Service of Medicine,' the motto of G. D. Searle & Co., expresses the emphasis management has placed on this function over the past two decades. The role of research in the company can be indicated by the number of patents awarded the

company, the number and level of personnel in research, and the proportion of total space allotted to research by the company.

"Approximately 44 per cent of the company's building area is allotted to research. The number of employees in research has doubled in the past five years alone. Today, over 200 of Searle's 900 employees are engaged in scientific research. Personnel in the research department includes three Ph.D.-M.Ds., two M.Ds., and 64 Ph.Ds. The balance of the department is divided between research technicians and non-scientific employees.

"As noted earlier, research at Searle has been channeled primarily toward the degenerative rather than infectious diseases. The company's research program may be classified as follows:

1. *Chemical Research* to discover and synthesize new molecules which will be therapeutically effective.
2. *Pharmacological Research* to establish in animals the effectiveness and toxicity of various chemicals.
3. *Clinical Research* to establish the therapeutic usefulness of drugs on humans.
4. *Product Research* to prepare marketable dosage forms for new products and improve the stability, appearance, solubility, etc., of drugs already on the market.

"Searle's research department, under the leadership of Dr. Raymond, director of research, is organized into three divisions—biological research, chemical research, and clinical research—each headed by a research director. As an aid to solving the ever-present risk of enmeshing top research scientists in day-to-day administrative detail, Searle has recently employed a manager of research personnel (separate from the company's personnel department). Dr. Raymond has also engaged an administrative assistant to handle much of the departmental detail. The research directors and Dr. Raymond systematically re-examine their own duties to assure ample time for the important planning necessary in an expanding department.

PAUL E. TILLMAN

"Integration and control of the research effort are accomplished within the department by means of three monthly meetings: a chemical research meeting, a biological research meeting, and meetings of a priority committee which continually readjusts the emphasis to be placed on each research project. Mechanisms exist also for informal discussion and

decision whenever necessary.

"Coordination of Searle's research with other divisions of the company and over-all research control are assured by a monthly research meeting, at which research progress is reviewed for all senior executives, and a monthly medical meeting, attended by top executives and the medical men from research and sales, which evaluates clinical reports in terms of sales potentials.

"Research expenditures are reviewed and compared with those of previous years by the president, senior vice-president, and director of research. Research expansion at Searle is restricted principally by the limited availability of the experienced senior scientists needed for the complex and relatively new areas it explores.

"Searle's research department and management's attitude toward it are close to ideal, in the Institute's opinion. The arrangement of research facilities and space provisions have been well planned for future expansion. The organization of the entire department, with representation at top management level, the various mechanisms for communication within the department, and the freedom with which important research is conducted earn this management the maximum rating in the Audit category Research and Development.

"Searle's board of directors consists of John Searle, president, the company's three vice-presidents, and five outside members. The board meets quarterly and the attendance is good. The board contains a diversity of occupational experience. Banking, insurance, law, education and medicine are represented by outside members; sales, research, production and finance by executive-directors. Almost all members of the board have excellent records of participations in business and professional activities beyond the limits of their own positions, as well as in national and civic affairs. The average of the directors is 57, and most of them are grouped closely around this age—a fact that undoubtedly contributes to the excellent working relationship among board members. . . .

"The company's financial affairs are handled chiefly by Paul E. Tillman, senior vice-president, and Kenyon D. Bowes, treasurer. Mr. Tillman retains over-all supervision of fiscal policies and outside financing, while Mr. Bowes is concerned primarily with internal financial matters, such as controllership, accounting, pensions, and insurance.

"Searle does not use any formal, company-wide budget system. . . . The nature of Searle's business and its emphasis and dependence on research militate against rigid budget arrangements. However, flexible budgeting would improve one important management function: forecasting and long range programming. The ability to project income and expenditures over the long term is essential to controlled expansion of plant and personnel.

"Many of Searle's controls are effected through a standard cost system. Cost variances are reviewed monthly by top executives and price and quantity variances are adjusted at that time. Strict financial controls are kept on purchasing and other departments. Perpetual inventories are kept and minimum limits reviewed constantly. Financial reports in the form of cash statements are made daily to top executives. In addition top management receives a written explanation for each disbursement over $1,000. The effectiveness of Searle's internal controls can be seen in the fact that the cost of goods sold has remained a relatively constant percentage of sales over the past twenty years, and selling, general, and administrative expenses have declined steadily in per cent of sales during the same period. *(Continued on page 135)*

FRANKLIN P. O'BRIEN

DR. ALBERT L. RAYMOND

Bath Preparations

Cosmetic Tranquilizers

by Joseph Kalish, Ph.D.

Aside from their primary cleansing purposes, showers and tub baths have long been known and used as "mood agents," a term which has in recent years been applied to drugs which affect the mood, either causing stimulation or relaxation. Men like to talk of the stimulation of a cold shower, although we suspect that the cold shower is more talked about than endured, but there is little question about its rejuvenating action in overcoming natural or alcoholic drowsiness. The warm b th, on the other hand, physically and mentally relaxes and soothes, an attribute of major value in mental hospitals. It is this rejuvenating relaxation that is pointed up in a current bath oil promotion: "You have had a hard day, filled with tension? You are tired, you are sad, you want to be beautiful, to have a lift, to come up smiling, a new fascinating, vital woman? It is so simple. When your bath is drawn, deep and really warm, spill in just as many of these golden drops as the bottle cap will hold. Now, immerse yourself, relax, enjoy what is happening to you—You do relax—you may even drowse a little. The magic is at work. And when you arise, like Aphrodite from the sea, you are a new woman. . . ." A pharmaceutical copy writer could say no more about a new ataractic.

Bath oils contain substantial amounts of perfume and can be formulated so that the latter is uniformly dispersed in the bath or is part of a thin, floating layer. A floating oil, which is the subject of the above-quoted promotion, offers attractive properties. It forms an occlusive layer over the surface of the bath water which retards evaporation and helps to maintain temperature; the perfume is at the surface instead of dispersed in the water and more effectively perfumes the atmosphere; a layer of perfume can adhere to the body; oils, formulated for cosmetic skin-softening action adhere to the skin. A bath oil of this type will consist of 20 per cent or more of the perfume compound dissolved in an oil or mixture of oils. The oil may be mineral oil or a suitable vegetable oil (along with an antioxidant) such as sesame or olive oil or a synthetic oil like isopropyl myristate, butyl stearate or a silicone. The addition of a lanolin oil or modified lanolin could provide both emollient and promotional plus values. A simple mixture of this nature would not necessarily spread over the surface of the water and would be likely to remain as large and small individual droplets; a spreading agent is required to complete the preparation. An oil-soluble surfactant, in which the lipophile or oil-soluble tendency is greater than the hydrophile or water-soluble tendency is called for and examples include higher aliphatic alcohols like octyl and lauryl alcohols whose odor may be intrusive, oleyl alcohol, cetyl and stearyl alcohols although their solubility is rather low, possibly cholesterol and non-emulsifying monoglycerides, and especially sorbitan fatty acid esters.

Dispersible bath oils are based upon sulfonated castor oil or other surface-active solubilizing agents.

EWING GALLOWAY PHOTO

They contain from 10 to 20 per cent of perfume oils and may also include fixed oils for emollience. Polyoxyethylene sorbitan esters are very effective in forming solutions with perfume oils that may be diluted to a considerable extent with water and still remain clear. The addition of vegetable or mineral oil makes the solubilization a more difficult problem and the resulting clear liquid will turn the bath water milky.

In considering the relative merits of floating versus dispersed bath oils, due consideration should be given to the bathing process. The tub is prepared, the bath oil is added, the bather steps in and, in the case of floating oils, her body acquires a coating of perfumed emollient oil. So far so good, but the final procedure involves thorough soaping of the body and rinsing, and it is hard to see how it is possible for much of the adherent oil and perfume to remain on the body, or for the oil film to remain intact in the presence of emulsifying soap. Small proportions of silicones may be helpful in this respect. Moreover, the oil film preparation is devoid of water-softening powers and in any hard water area the usual bath-tub ring will be intensified by the added oil. In the case of the dispersed oil, on the other hand, additional dispersing agent can be present to a sufficient extent to disperse the hard water curds and prevent bathtub ring formation. We believe then, that bath oils are presently useful products in terms of their utility and promotional values, but more investigation is required to bring about peak performance in both of these aspects.

From the beginning, an aura of luxury and relaxation has accompanied the use of bubble baths, and only excessive cheapening of the products has retarded their growth. Actually, a product can be properly formulated so that it is both good and relatively inexpensive. Its usefulness is real, as well as subjective, since the hard water soaps formed as a scum by the interaction of lime and magnesium salts and the sodium salts of fatty acids are dispersed by these surface active agents and are no longer adherent to the body and to the sides of the tub. These preparations are available as powders or as liquids, both based upon high-foaming surface-active agents.

The general classes of active ingredients include the fatty acid alkylolamide condensation products, otherwise used as foam stabilizers in shampoos, fatty alcohol sulfates, aralkyl sulfonates, aralkyl polyethers and recently, fatty alcohol polyether sulfate. All of these produce adequate foam with distilled or soft water, the aralkyl ether possibly being somewhat less effective than the others. Hard water has an adverse

(Continued on page 108)

TABLET COATING ...Wet and Dry*

by Jack Cooper and William Gunsel

RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS INC., SUMMIT, N.J.

Coating began in the United States when Warner, a Philadelphia pharmacist, began dipping capsules in syrup.[16] The first coated pills were prepared by impaling the pills on needles and dipping them into a coating syrup. Later a suction device was perfected which held them while one half of the surface was coated. Then the pills were reversed and the other half dipped. Tablet coating developed from pill coating, the major forward step being the use of the revolving pan.

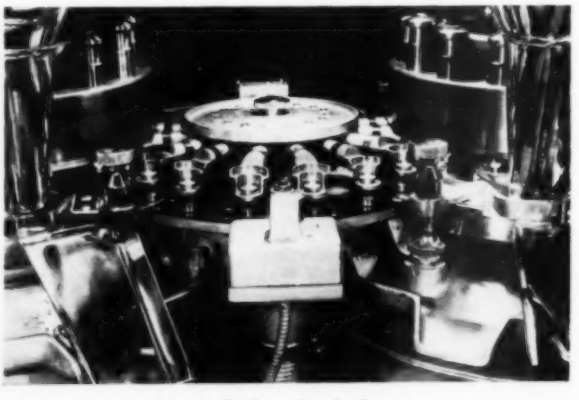
The following reasons for coating tablets are representative of the many advanced by proponents of the procedure:

1. Coated tablets are esthetic in appearance. One might even suggest blue coated tablets for depressions and red coated tablets for heartburn and yellow tablets for jaundice.
2. Coated tablets are easier to swallow because of their smooth, unbroken surfaces. This is probably more psychological than physical because many people have more trouble swallowing a smooth raw oyster than a rough fried one.
3. Protection of the tablet from humid climates. This advantage is dubious since sugar coatings deteriorate rapidly in the presence of high humidity.
4. Coated tablets provide a barrier between the taste buds and an unpleasant tasting drug.
5. Enteric coated tablets protect sensitive drugs from attack by stomach juices.
6. Enteric coated tablets provide release of the drug in concentrated form in the intestines.
7. Delayed action tablets provide therapy without interruption of sleep. This advantage applies only in those cases where therapy other than sleep is indicated.

Coating actually begins with the preparation of the cores or nuclei. Ideally these should be hard, with dense surfaces; the edges should be thin and the surfaces very convex (11-15). Thus the coating solutions will not readily soften the tablet and the rounding of the edge will be facilitated.

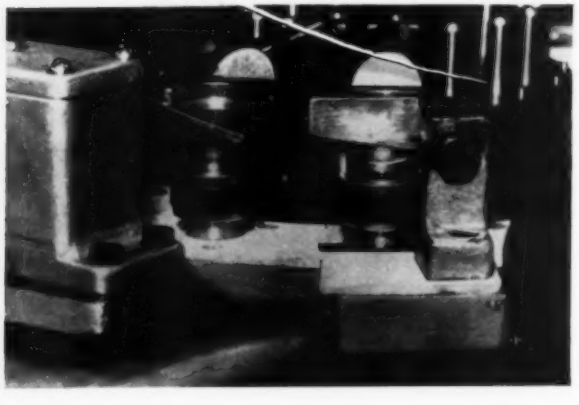
The four essential steps in coating include undercoating or subcoating, smoothing, finishing and polishing. The subcoating consists of a heavy syrup containing flour or a gum and is intended to form a bond between the nucleus and the outer coatings. It is usually applied very hot and dusted with some insoluble materials for rapid increase in weight. Dusters commonly used contain starch, talcum, calcium carbonate, magnesium oxide, powdered sugar and acacia. If the cores are hygroscopic or tend to be soft, one or two coats of a waterproof substance are applied first.

The purpose of the smoothing coat is to render uniform the surface of a tablet which although rounded

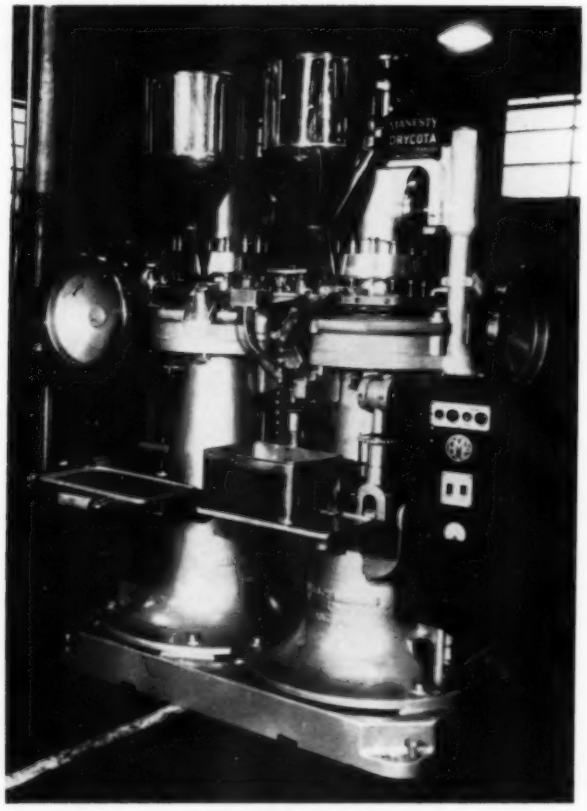


Manesty DryCota, Transfer System

Manesty DryCota, Rear Microswitch



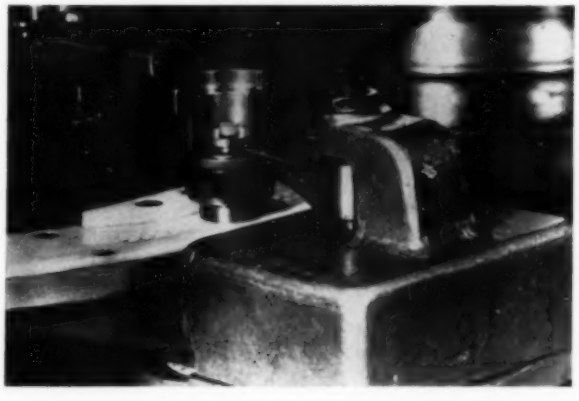
*Presented at the annual meeting of Production Section, Canadian Pharm. Mfg. Assoc., Detroit, Michigan, April 27, 1956.



Manesty DryCota, Front View

by the subcoating operation is still irregular. The solution used is a heavy sugar syrup applied at 140-150° F. and dried with warm air. If the tablets are to be finished white, large amounts of opaque substances such as calcium carbonate may be added to the syrup. For color coating a somewhat lighter syrup is employed with increasing concentrations of color as the coating continues. When the tablet has reached the desired shade, two or three coats in reduced quantity are drizzled on the tablets and dried without air until they have a flat, dull appearance. The tablets may now be removed from the pan to trays for overnight drying or may be dried out in the pan

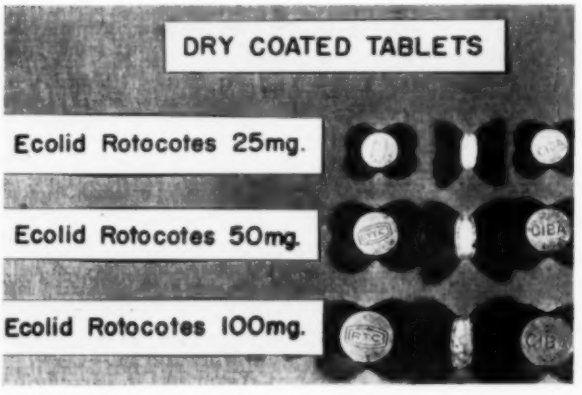
Manesty DryCota, Front Microswitch



for two or three hours. In the latter method, the pan is stopped and covered. It is then rotated approximately one quarter turn every five minutes for the desired time.

After drying, the tablets are placed in polishing pans or drums. The former is actually a coating pan which has been lined with wax or canvas impregnated with wax. The latter is a round canvas form held taut by metal rods. The waxes used are Carnauba or beeswax or a combination of the two[21] in a solvent such as gasoline, naphtha or carbon tetrachloride. The solution is poured on the tablets which are then rotated until a high gloss develops.

Even the most expert coater will produce a batch of bad tablets due to mottling. The causes of mottling are several: the tablets may not have been completely dried during the coating; they may not have been completely smoothed; the color may have been too concentrated; a chemical reaction may have occurred between the drug and the color. It is customary at such times to salvage the tablets by washing off the coating either part way or all the way to the core. To do this it is necessary to have a basket of wire mesh, a bucket of warm water and a bucket of denatured alcohol. Several pounds of tablets are loaded into the basket and the basket agitated in the warm water until the edges of the nuclei appear. The basket is then plunged into the alcohol which absorbs some of the water. Some coaters dunk the tablets in cold water before using the alcohol bath. The wet tablets are dumped into a coating pan and rotated under a a full blast of hot air until dry. The first batch washed



must be stirred by hand until the tablets roll freely. Successive basketsful will separate much more easily because some of their moisture will be absorbed by the already dry tablets.

A method suggested in 1950[36] uses a Stokes polishing pan from which the canvas has been removed and replaced with wire screening. Drain boards are arranged to catch the washings. Sixty to eighty pounds of tablets are placed in the drum and the machine set in motion. Forty-five per cent isopropyl alcohol is slowly poured over the tablets until the edges ap-

(*Continued on page 108*)

The Sphere of Research*

by Paul G. I. Lauffer
CHIEF CHEMIST, THE GEORGE W. LUFT COMPANY, INC.

Numbers one to twenty-four inclusive of the *Proceedings of the Scientific Section of the Toilet Goods Association* contain 205 papers, by 225 different authors. One author's name appears on six papers, three on five papers, seven on four, nine on three, and twenty-eight on two.

The sources of papers were:

Toilet Goods Industry	64
Suppliers	56
Consultants	45
Universities	20
Government	16
Other Industries	5
Physicians	4
Publications and Advertising	3
Attorneys	1

The papers dealt with the following subjects:

Ingredients (Total 66)	
Essential Oils and Aromatic Chemicals	13
Surfactants	11
Packaging Materials	7
Thioglycolic Acid, etc.	6
Germicides	5
Humectants	5
Solvents	5
Colors	3
Petrolatum	3
Stearic Acid and Stearates	3
Other Materials	5
Product Testing (Total 54)	
Testing for Safety	24
Testing for Efficacy	16
Testing for Acceptability	12
Testing for Stability	2
Odor & Olfaction	10
Monographs on Cosmetic Preparations	8
Cosmetics and Dermatitis	5
Dermatology	5
Dentifrices	5
Aerosols	3
Manufacturing Technique	3
Microscopy	3
Perfumery	3
Statistics	3
Formulation	2
Hair Growth	2
Mech. Behavior of Hair	2
Halitosis	2
Pharmacology	2
Regulations	2
Aging	1
Education	1
Management	1
Marketing	1
Patents	1
Perspiration	1
Odor Classification	1
General	1

As shown in the above tabulation, the two topics most discussed in this Section were product testing for safety and product testing for efficacy. This fact reflects the constant concern of the cosmetic manufacturer with the formulation of more effective cosmetic products and the maintenance of high standards of safety. In addition to the twenty-four papers dealing with safety tests and the sixteen on efficacy, many of the other papers dealt to greater or lesser extent with these subjects.

The wide variety of topics attests the manifold nature of the constant effort, in the many laboratories of the Toilet Goods industry, to advance cosmetic art and science. The advance is limited only by the incompleteness of the underlying sciences, and the more progressive laboratories are undertaking studies of sufficient depth to contribute to these underlying sciences.

The discovery that man's habitation is the surface of a sphere has had a profound influence on concepts far outside the bounds of geography. By assigning a finite size to the earth, new hopes were born of its eventual complete exploration. The universal brotherhood of man became a possibility, one that has as-

*From proceedings of the Scientific Section of the Toilet Goods Association, No. 25. May, 1956.

COURTESY WYANDOTTE CHEMICALS CORP.

sumed ever greater meaning with shrinking of distance by speedier travel and instantaneous spreading of news. Analogously, the many technologies occupying human effort may be considered to be related and of finite extent, and the body of scientific knowledge underlying them is more compact and harmonious, especially as its more fundamental principles come to light.

The entire field of technology may be likened to an area on the surface of a sphere, with the underlying sciences making up the sphere's interior. The model sphere is composed of almost opaque, but very slightly translucent, material, and has a powerful light source at its center. Superficial work in any technology is done largely in the dark, for it does not penetrate deeply enough to shed adequate light on a problem. Studies which dig deeply enough to uncover scientific principles shed bountiful light on the problem under study, and on neighboring technologies.

As cosmetic chemists dig deeper into the scientific strata, their tunnels cross those of workers from other fields. They obtain light from the discoveries of investigators who have approached from other angles. The deeper they dig, the closer they come to other workers. The more fundamental scientific discoveries cast light upon wide sectors of the whole technological field.

The problems in pure science which we as cosmetic formulators wish to have attacked are so many and so formidable that we have not at our disposal the means for effectively attacking all of them in depth, unaided. Fortunately the laboratories of other industries, universities, research institutes, and governmental agencies are working on many problems which shed light on cosmetic technology. One example may serve to indicate how far-reaching and beneficial the consequences of a single scientific achievement may be. This achievement, still in the realm of things hoped for, is adequate explanation of the structure and functioning of enzymes and other protein compounds.

Many practical problems encountered in the technologies of chemotherapy, public health, nutrition, and cosmetology cannot be adequately solved until further knowledge of proteins permits their solution. A great deal of scattered effort has been expended on protein and enzyme studies, and dozens of books and thousands of papers have been written on the results. Much light has been shed, but here are a few of the things we still do not know:

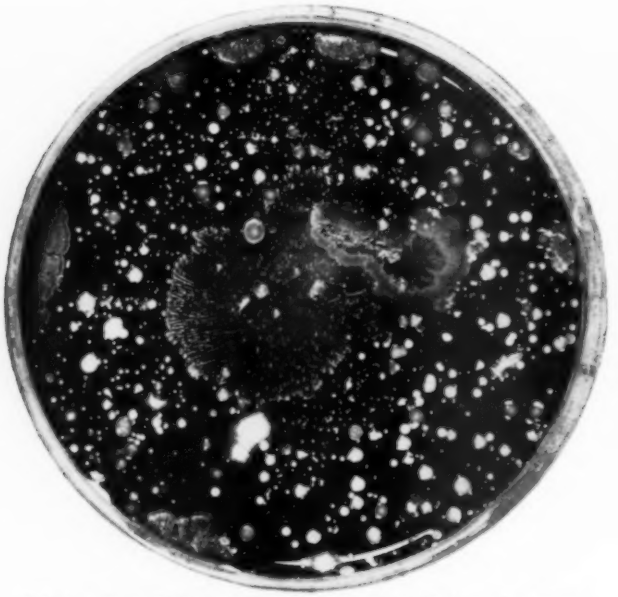
1. Detailed chemical and geometrical structures of the important proteins of the body, including those of the skin. We know that skin proteins such as keratin, collagen, and elastin are of prime importance, but we do not have adequate knowledge of their structure, how they change with age, nor how such changes and other harmful effects may be retarded.

2. The mechanism whereby chemical substances alter proteins to produce skin sensitization. We do

(*Continued on page 124*)

KISSING HYGIENE

by Dr. Arthur H. Bryan
CITY COLLEGE, BALTIMORE 18, MD.



Colonies of mouth bacteria, washed from the mouthpiece of a cornet and allowed to grow out for ninety-six hours at room temperature on blood agar plates. Most are harmless, particularly the large colonies.

Mouthpieces of wind instruments harbor possible viruses and millions of bacteria from the mouth, according to the author, shown above with three of his students in the bacteriology laboratory.

Then there's that proverbial hypochondriac, germ conscious maiden who takes the joy out of kissing, by meticulously spraying her throat and lips before and after each osculation, and worse still, she requires her copartner in lip contact to do likewise. Is she justified in her prophylactic proceedings?

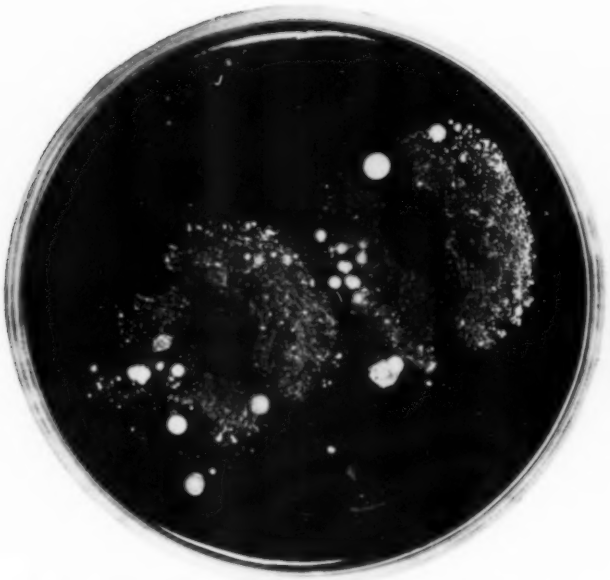
To answer the age old query as Shakespeare might phrase it "To kiss or not to kiss that is the question;" some simple quantitative experiments were carried out to determine the extent and kinds of bacterial and viral growth on the lips and in the mouth.

Human guinea pigs, both male and female, with and without colds, fever blisters or cold sores, with and without lipstick, smokers and non smokers, before and after mouth washing and tooth brushing, dry versus moist lips, etc., impressed their reluctant lips for varying periods from one to ten seconds on sterile slides, or culture media and the microbial flora was studied and evaluated. Mouths were washed out with sterile water or gargling practiced for ten seconds and the resultant expectorant plated on nutrient media so that the living microorganisms would grow and multiply to eye-visible colonies. The mouth and lip plates were incubated for twenty-four to forty-eight hours at body temperature, when numerical and differential colony counts were made, and possible disease inciting bacteria classified and identified. Then from the statistical data and comparative results, so obtained, some presumptive and tentative conclusions were drawn. Five different techniques were used, and the combined results were compared and evaluated to warrant the conclusions which follow.

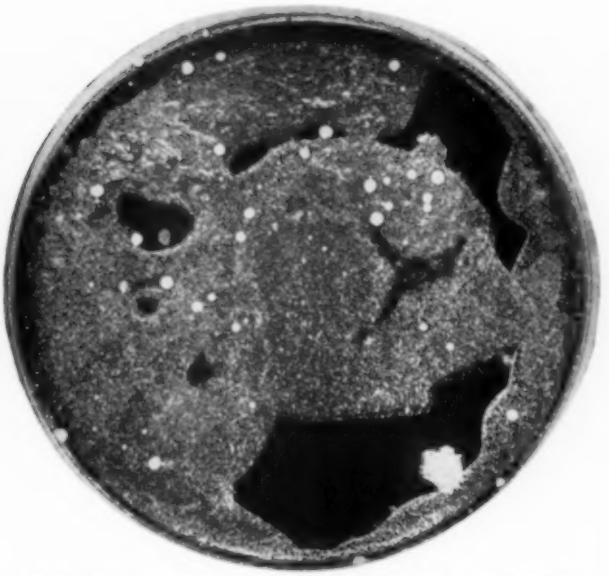
In addition, the author's eleven published scientific papers on correlated topics were reevaluated in connection with their bearing on the present problem. To economize on plated culture media on which the mouth and lip bacteria were grown, the plates were divided into four quarters, and lip impressions made on each quarter.

The number of colonies of bacteria per pair of double lip impressions varied from 25 to over 278 with a ratio of over 1:5 rough to smooth colonies.

With the viruses, kissing may be the fomite of in-



Bacteria transferred from lips of two males to blood agar plates during five-second impressions. The small colonies were transferred directly, the large white colonies may be air-borne.



Washed from the mouth of a male, these colonies can be transferred by prolonged oral osculation and can, when resistance is low, incite upper respiratory infections. Black areas were not covered by the wash.

Blood agar culture of mouth and lip bacteria washed from the mouthpiece of a clarinet. Staphylococci, streptococci and pneumococci are represented. (Note hemolysis zone at five o'clock.)

fection in colds, influenza, virus "X," viral and pneumococcic pneumonia, and upper respiratory infections, etc.

Clinical experience revealed that fever blisters, cold sores (herpes fibrilis), can be definitely transmitted by prolonged osculations.

The number of bacteria transferred from lips to culture media was directly proportional to how long a single kiss lasted. A regulation Hollywood ten-second-kiss transferred almost twice as many germs as a short two-second affair.

Dry lips harbored consistently fewer bacteria than moist.

The bacterial flora was consistently higher upon rising in the morning and dropped considerably after completing the usual morning toilet (mouth wash, tooth brushing, soap ablutions of the face), and in women after fresh lipstick application.

Alcohol beverage drinking gave inconclusive results with the few samples taken. However beer appeared to raise, and hard liquor to lower the comparative data germ counts.

High bacterial lip counts and bad breath showed a very positive correlation. Sweet lips and sweet breath make a good team bacterially speaking.

Low bacterial counts were directly proportional to odorless breath (garlic and onion odor possibly excepted).

The kiss of death is a distinct hazard when fatal infections such as: meningitis, diphtheria, scarlet fever, phthis, acute pulmonany tuberculosis, hemolytic strep throat, etc., are involved.

Over 95 per cent of the lip flora of bacteria were avirulent, hence non-disease inciting. They exist apparently as harmless commensalists.

Kissing can be not only a pleasant, but a harmless pastime if ordinary lip and oral hygiene is practised, and that irrespective of the frequency or how long the contact lasts.

Antiseptic men's lipstick is an excellent prophylaxis against fever blisters and cold sores, pathogenic micrococcia and other possible lip transmitted infections.

Women's lipstick tends to accomplish the same effects as men's. If they want added safety, a mild, non-irritating pleasant tasting antiseptic might be incorporated in some lipsticks by interested manufacturers.

The ideal antiseptic in a lipstick, male or female, should be cool, non-irritating, inhibitory, not neces-

(Continued on page 134)

COURTESY HELENA RUBINSTEIN

Shampoo Evaluation*

by W G. Fredell and R. R. Read

LAMBERT-HUDNUT DIVISION OF WARNER-LAMBERT PHARMACEUTICAL CO.

Shampoos are designed to clean the hair and scalp. In most instances, people associate the idea of abundant lather formation during this operation as a criterion of efficiency. Usually, if one uses a large enough quantity of any lathering shampoo product, one can obtain an abundant lather. Because this property of lathering seems to be important to users of shampoos today, our studies in this field have resulted in an *in vivo* method which gives duplicable results. Since, in addition to cleansing, a shampoo user desires a good appearance of the hair after the operation, lack of residues could contribute to that good appearance. An *in vitro* method was evolved to study this point and will be described.

Users of shampoos cannot evaluate lathering power of shampoos on the basis of a shampoo at home once or twice a week because the conditions and contamination can be so variable, nor can casual subjects be used in the laboratory. The amount of soil on the hair is one of the biggest variable factors. Hair dressings may be applied some times and not others. If these are oily, they will suppress lathering. Dirt, dust, and other air born soil can soil a head of hair and suppress lathering. Recognizing these factors, we set out to standardize a method. At first, we attempted to classify the amount of lather produced by increasing weights of shampoo on standardized heads of hair.

*From proceedings of Scientific Section of the Toilet Goods Association, No. 25, May, 1956.

Table I—Typical Shampoo Test Results

Subject	Product	Amount of Shampoo Used in Grams: Before Rinse	After Rinse	Total
201	A	0.75	0.5	1.25
	A	0.5	0.5	1.0
	B	0.75	0.5	1.25
	B	0.75	0.5	1.25
	C	1.0	0.5	1.5
	D	0.75	0.75	1.5
	E	0.75	0.5	1.25
	F	0.75	0.5	1.25
	G	0.75	0.5	1.25
203	A	1.0	0.5	1.5
	B	1.0	1.0	2.0
	D	2.5	0.75	3.25
	E	1.5	0.75	2.25
205	A	0.75	0.5	1.25
	A	0.75	0.25	1.0
	B	1.75	0.75	2.5
	B	1.5	0.5	2.0
	C	1.0	0.5	1.5
207	A	0.5	0.5	1.0
	C	1.0	1.0	2.0
	D	1.0	1.0	2.0

A, B, and C are commercial cream shampoos
D and E are commercial liquid shampoos
F and G are detergent only products containing the same concentration of detergent as Shampoo A but F buffered to a pH of 9 and G to a pH of 4.
To illustrate the relationship of soil to amount of shampoo required, a subject applied 5 cc. of the hair soil. The results obtained using 1 gm. portions of shampoo C were as follows:

1st application of 1 gm.—no lather
2nd application of 1 gm.—no lather
3rd application of 1 gm.—no lather
4th application of 1 gm.—no lather
5th application of 1 gm.—sparse lather—fading
6th application of 1 gm.—medium lather
7th application of 1 gm.—abundant lather

After more than 250 shampoos on men's heads of hair, the subject being his own control, we adopted the following procedure.

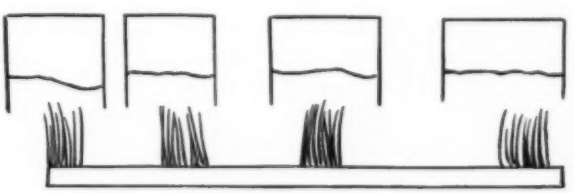
The subject shampoos initially to produce an abundant lather. After thorough rinsing and drying well with a towel, 2 ml. of a standard hair soil are pipetted onto the head and distributed by rubbing. The subject is now ready when the hair is dry to use the shampoo under test. (We used a hair soil composed of 20 per cent Anhydrous Lanolin and 80 per cent light Mineral Oil. The test method lends itself to the use of any type of soil or hair preparation).

The subject uses 0.25 gm. of the shampoo under test and attempts to work up a lather. The hair is wetted first and water added as needed. If no lather appears, additional 0.25 gm. portions of shampoo are applied and rubbed well in order to produce a lather until a permanent lather is produced. (In observing this shampooing technique, a slight build up of lather is frequently noticed which quickly fades. Hence, a permanent lather must be worked up.) The hair is rinsed and additional 0.25 gm. portions of shampoo used until an abundant lather is produced. This lather is rinsed off thoroughly, the hair dried with a towel, and 2 ml. of standard hair soil added to the head of hair and distributed by rubbing. The subject is set up to be used again on another product for comparison, and so on.

The method is essentially a titration of a standardized soiled head of hair with 0.25 gm. portions of shampoo to an endpoint of a permanent lather. That is, a lather that remains for about a minute. The hair and scalp can be clean at this point but because many people are sold on rinsing the first lather off and applying more shampoo to work up an abundant lather, the test method continues with this operation. (This entire shampoo operation only takes about seven minutes.) Table I shows some typical results of this method. The subject need not know which product is being used as a technician weighs out the 0.25 gm. samples of shampoo on cellophane weighing papers and applies them to the head. Two or three observers, including the subject looking into a mirror concur on the lather produced. The subject usually shampoos in the same manner each time. Different subjects have different techniques hence he is used as his own control.

With respect to residues remaining on the hair after a shampoo, a simple *in vitro* test has given some rather startling results. Swatches of about 100 hairs six inches long were taken from women who had relatively recent beauty shop permanents. By selecting a swatch from one area representing a uniform curl which had, no doubt, been rolled on the same curler during the waving process, we felt that we had uniform samples of hair. The hairs from a swatch were individually mounted, scalp end only, and arranged in groups of ten hairs each and spaced along an applicator stick as per the following diagram.

Shampooing was carried out on four or five groups of ten hairs each simultaneously by dipping them repeatedly in two per cent solutions of different shampoos contained in 4 oz. jars as illustrated.



The operator using an up and down motion washed the groups of hair for two minutes in the respective shampoo solutions which had been stored in a 37.5° C. oven prior to use. After the shampoo treatment, the groups of hair were rinsed twice for one minute each in separate jars of water, also warmed by storage in the oven. Then, matting and tangling were straightened out using the end of an applicator stick.

(An applicator stick was used to disentangle the hairs because a comb was found to pull matted hair too much and could dislodge residues deposited on the hair.) The groups of hair were hung up to dry and then observed with the naked eye for residues. Results of testing a number of shampoos are given in Table II.

(Continued on page 133)

Planning the Research Program of a Pharmaceutical Company*

by T. F. Davies Haines
PRESIDENT, CIBA PHARMACEUTICAL PRODUCTS INC., SUMMIT, N. J.

The first installment of this two-part abstract of Mr. Haines' talk included his observations on factors governing research programs of drug manufacturing companies: (a) Need of Continuity of Support; (b) Size of the Research Budget; and (c) Diversity of Scientists Required for Pharmaceutical Research.

(d) *Outside Research v. Company-conducted Research*

In addition to fixing the over-all size of the research budget and appropriating the funds needed to provide laboratories, pilot plants and the like, there is one other function that the board of directors should perform in planning the research program. That is deciding how much of the research budget should be spent on research conducted in universities, medical schools and independent foundations on projects that are largely within their own discretion and how much on research to be done in the company's own laboratories. I say advisedly "projects that are largely within the discretion" of the independent agency to distinguish them from clinical testing of the company's own products which must usually be done in independent hospitals and clinics and which is ordinary routine for a pharmaceutical company.

In addition to grants for this normal routine clinical research, some companies have made substantial grants to independent agencies for research which is not connected with the clinical testing of products which the grantor hopes to introduce to the market. The company for which I work has adopted such a policy. It has done even more. In 1947 it established in London the CIBA Foundation for the Promotion of International Cooperation in Medical and Chemical Research, and has subscribed increasingly large amounts for its annual support ever since. The Foundation is directed by trustees who are wholly independent of CIBA and can carry out any projects they may see fit provided that they fall within the broad purpose of the Foundation which is described in its charter to be

> "to advance and promote the study of and research in all branches of the sciences of chemistry, medicine and surgery and in particular to advance and promote international cooperation in medical, chemical, biological and pharmaceutical research."

The Foundation even in the few years of its existence has produced results of real value, and many universities, medical schools and other scientific organizations in the United States and abroad are today engaged in fruitful research projects, which derive their original stimulus and inspiration from the Foundation.

(e) *Fields of Interest of the Research Scientists*

Next to the size of the research budget the factor which has the greatest influence on the selection of the fields in which to concentrate the research effort is the range of the interests of the leading scientists, both the leading chemists and the leading biologists, in the Research Department. Because of the complexity of the scientific problems involved in medicine, lay members of the board of directors or of the management could not arrive at informed decisions as to the relative amounts of laboratory effort which could justifiably be devoted to one or another possible field of investigation. The risk is thus inherent that large amounts may be spent on one line of products while another line is largely neglected.

The result has been that many pharmaceutical companies have tended to specialize in certain fields. A company which has not yet entered the vitamin field would be unlikely to number among its staff scientists interested in the field of nutrition. If, however, its staff includes steroid chemists, much work may be concentrated on modifying naturally-occurring hormone molecules to make more active and possibly less toxic products, such as the recently discov-

*Presented before Conference on Industrial Research, Harriman Campus of Columbia University, June 12.

COURTESY CIBA PHARMACEUTICAL PRODUCTS INC.

ered cortical-type hormones which do not exist in nature and which are proving superior to the natural products for the treatment of arthritis and many other diseases. Other chemists may find their principal interest in the study of alkaloids, complex basic substances found in plants and represented by such typical members as nicotine, atropine, quinine, morphine, strychnine and the recently discovered reserpine. Synthetic chemistry has been able to modify advantageously the molecular patterns of certain of these substances and thus build up new molecular patterns having more useful medicinal properties than the naturally occurring compounds or otherwise fulfilling specific physiological requirements. Examples are the discovery of the synthetic quinine substitutes for the treatment and prevention of malaria and the atropine-like products which have been synthesized for the treatment of stomach ulcers and other gastric disorders. Chemists principally trained in the fermentation field may work largely on the discovery and commercial production of new antibiotics.

There is, of course, much over-lapping of the work in these different fields. Witness, for example, the production of steroids by fermentation processes, the discovery of vitamin B_{12} as a by-product of streptomycin fermentation, etc. Moreover drugs developed primarily to treat one disease have not infrequently been found to have totally unexpected uses. Examples are certain antihistamines originally developed to treat allergic conditions which were later found to be good remedies for motion sickness, and reserpine originally used to reduce blood pressure and now found to have dramatic effect in the treatment of mental disorders.

Not all research achievements, of course, begin with the study of the pharmacological effects of newly synthesized chemical compounds or with the broad screening of thousands of substances such as is done in the search for new antibiotics. Many of the major discoveries of the past, and many of those now in the offing, have had and will have their genesis in the basic study of the cells and organs of which our bodies are composed. Basic studies of the various types of cancer cells and viruses may well lead eventually to the discovery of specific therapy in these areas.

These few examples must suffice to illustrate the vastness and complexity of the fields open to medical and pharmaceutical research and why it is the research scientists themselves, and not lay members of the management, who must select the projects to be included in the research program. They show that what cannot be done is to plot out in advance research in areas which in the eyes of the market research men promise the broadest markets and the greatest freedom from competition, or in which patent protection is most likely to be obtained, or which otherwise have the most attractive prospects for a high dollar return on the research investment. Such an approach to research planning is quite possible in some lines of business, but not in the pharmaceutical industry. We simply do not know enough about the selective nature of drug action or the general relationships existing between molecular structure and physiological effect. This accounts for the fact that, as already stated, there is a high degree of empiricism in pharmaceutical research and that progress largely depends on the

(Continued on page 129)

DEPILATORIES

by Harry Hilfer

The safe and easy removal of unwanted hair has been a problem which modern women have been faced with since it became fashionable to wear short skirts. The use of the razor in covering an area as large as the surface of the legs is rather tedious and awkward. Therefore products which enable hair to be removed with a minimum of effort are still much in demand. Chemical depilation is dependent on a reduction of the hair molecule in conjunction with a swelling of the hair shaft usually brought about by an alkaline medium. Specifically, the reduction is made on the cystine position of the hair molecule, breaking the disulfide linkage. Alkali then presumably reacts with the sulfhydryl groups formed causing the swelling and weakening of the shaft to take place, to a point where the hair may be removed by gentle massage.

In tracing the development of the chemical depilation agents, it is not surprising to find that sulfides were among the first reducing agents to be used. Since an alkaline medium was also necessary, the choice evolves to the sulfides of the alkaline earth metals. These preparations were usually sold in a powder form accompanied by instructions for preparation of an aqueous paste prior to use, since most of the alkaline earth sulfides have a tendency toward hydrolysis in water with the evolution of hydrogen sulfide. This, of course, will not happen in the absence of water. The alkaline earths have the further advantage in forming hydroxides of relatively low solubility and for this reason keeping the alkalinity within non-irritating bounds. Strontium sulfide, particularly, was in great general use for this purpose because it seemed to do a fast depilation job with minimum irritation. The pH at which depilation seemed to go most quickly was at about 12. At a pH of 11 depilation was too slow to be satisfactory.

In conjunction with the pH problem inherent in depilatories, a pH of 12 indicates a high alkalinity and is usually thought of as unsafe, but if the time of exposure to the skin is short, irritation is so low as to be insignificant. Actually it is safer to subject the skin to an exposure of pH 12 for about four or five minutes, then to pH 10 or 11 for several hours. A seemingly high pH therefore brings no great irritation hazard unless exposure is unduly long. Other alkaline earth sulfides in use were the calcium sulfhydrate principally and sodium sulfide (usually used to accelerate the activity of the alkaline earths). Soluble barium salts are regarded as toxic and, though barium sulfide is a good depilation material, its use was considered hazardous. Zinc sulfide on the other hand is too insoluble to be effective, while magnesium sulfide forms an hydroxide which is too weakly alkaline.

These preparations in addition to the sulfide have incorporated in them fillers which enhance the formation of an aqueous paste. Actually, the amount of the sulfide added is usually less than 10 per cent of the total, the remainder being talc, kaolins and other substances which are good absorbers of water.

The sulfides all suffer from the fact that hydrogen sulfide is evolved when they are mixed with water, and though they were in fairly common use and they were effective, the odor of H_2S is not exactly conducive to a good esthetic appreciation. Obviously, there are other reducing agents which presumably could effect the depilation of hair without being so malodorous. Stannites are an example, since there is a wealth of work done along these lines as is evidenced by the patent literature. However, they have never been quite successful commercially—possibly because the depilation time is not as rapid as the more generally used sulfides.

More recently attention has been centered on organic sulfides which, to a great extent, eliminate the objections found in the metallic sulfide. These are possessed of good reduction potential and may be used at a pH great enough to enable rapid depilation to take place. The most notable of this class are the

(Continued on page 136)

COURTESY PELLEX CO.

Quantity Tolerances in Packaging Shipments

Quantity tolerances in shipments of various types of packaging materials is the subject of Advisory Service Report No. 347 issued last month by the Packaging Institute. The report is a compilation of information received from 110 corporate members of the Institute in answer to questionaires. The report is broken down into several categories of users, and information is also given as to the quantity tolerances of suppliers. Quantity tolerances of packaging materials are reported for three different types of orders: First, for standard items on which repeat orders are likely; secondly, for special items with few repeat orders; and thirdly, for packaging material from the manufacturers' stock.

The report on manufacturers of drugs and pharmaceuticals is based on returns from twenty manufacturers in this category. The report on manufacturers of cosmetics and toiletries is based on ten manufacturers in this category, but also includes four in the chemical field, two manufacturers of cleansers, and one in the textile field.

The report on the suppliers of packaging materials is based on reports from a total of 43 manufacturers in this category. These include manufacturers of bags, adhesive and tape, collapsible tubes, closures, cans, folding boxes, shipping containers, paper, glass, and film and foils.

The complete report is available from the Packaging Institute, 342 Madison Avenue, New York 17, at $3.00 per copy for members of the Institute, and $5.00 for non-members.

DRUGS AND PHARMACEUTICALS

	Standard Items Repeat Orders Likely			Special Items Few Repeat Orders				Packaging Materials from Manufacturer's Stock		
	per cent limit on			per cent limit on overrun for				1. is nearest full case o.k.? 2. if yes, what per cent?		
	Over Run	Under Run	Number of Companies	5M-50M	50M-500M	Over 500M	Number of Companies	#1	#2	Number of Companies
	10	10	9	10	10	10	3	Yes	10	5
				10	10	5	1			
	10	4	1	10	8	5	1	Yes	Not	7
	10	0	3	10	5	5	1		LTD	
	5	5	3	10	5	3	1			
	0	0	1	10	5	2	1			
Closures				10	5	1	1	Yes	LTD	1
				5	3	2	1	Yes	50	1
				2	1	1	1	Yes	15	1
				2	1	½	1	Yes	5	1
								No	x	1
	15	15	1	15	8	5	1	Yes	50	1
	10	10	8	10	10	10	3	Yes	15	1
								Yes	10	4
				10	10	5	1			
	10	5	1	10	8	5	1	Yes	5	1
Glass Containers	10	0	2	10	5	23	1	Yes	Not	
	5	5	3	10	5	1	2		LTD	1
	2	2	1	3	2	2	1	Yes	LTD	1
	0	0	1	2	1	1	1	Yes	Not	5
				2	1	½	1		LTD	
				1	½	¼	1			
				0	0	0	2	No	x	1
	10	10	8	15	5	3	1	Yes	50	1
				10	10	10	4	Yes	15	2
								Yes	10	3
	10	5	1	10	8	5	1			
	10	0	4	10	5	3	1	Yes	5	1
Folding Cartons				10	5	1	1	Yes	LTD	1
	5	5	2	5	3	2	1	Yes	Not	2
	1	0	1	5	2	1	1		LTD	
				3	3	3	1	No	x	1
				2	1	1	1			
				2	1	½	1			
				2	x	x	1			
				0	0	0	1			
	15	15	1	15	5	3	1	Yes	50	1
	10	10	8	10	10	10	4	Yes	15	2
								Yes	10	3
				10	8	5	1			
	10	0	3	10	5	3	1	Yes	5	1
Set-up Boxes				10	5	1	1	Yes	LTD	1
	5	5	2	5	2	1	1	Yes	Not	
	2	0	1	3	2	2	1		LTD	2
				2	1	½	1	No	x	1
				0	0	0	1			
	20	20	1	20	10	5	1	Yes	50	1
	10	10	8	10	10	10	3	Yes	15	1
								Yes	10	3
				10	10	5	1			
	10	5	1	10	8	5	1	Yes	5	1
	10	0	3	10	5	3	1	Yes	LTD	1
Shipping Containers				10	5	1	1	Yes	Not	
	5	5	3	5	2	1	1		LTD	2
				3	2	2	1	No	x	1
	2	2	1	2	2	2	1			
				2	1	½	1			
				1	x	x	1			
				¼	⅛	x	1			
				0	0	0	2			
	20	20	1	20	20	20	1	Yes	50	1
	20	0	1	20	10	5	1	Yes	15	1
	10	10	7	10	10	10	3	Yes	10	3
				10	8	5	1	Yes	LTD	i
Labels	10	5	1	10	5	5	1	Yes	Not	
	10	0	3	10	5	3	1		LTD	2
				5	3	2	1	No	x	1
	5	5	1	3	3	3	1			
	1	0	1	2	1	½	1			
				2	x	x	1			
				0	0	0	1			
	10	10	8	10	10	10	3	Yes	50	1
								Yes	15	1
				10	8	5	1	Yes	10	3
	10	5	1	10	5	3	1			
Tape	10	0	2	10	5	1	1	Yes	LTD	1
	5	5	1	5	x	x	1	Yes	Not	3
	0	0	3	2	1	½	1		LTD	
				0	0	0	4			
								No	x	3
	10	10	7	10	10	10	2	Yes	50	1
				10	8	5	1	Yes	15	1
				10	5	3	1	Yes	10	2
	10	0	2	10	5	1	1	Yes	Yes	Under-run 1 LTD
Adhesive	0	0	6	2	1	½	1			only
				0	0	0	6			
								Yes	LTD	1
								Yes	Not	4
									LTD	
								No	x	3
	10	10		10	10	10	4	Yes	50	1
								Yes	15	1
				10	8	5	1	Yes	10	3
	10	0		10	5	3	1			
				10	5	1	1	Yes	5	1
Metal Container	5	5		10	x	x	1	Yes	LTD	1
	2	2		5	x	x	1	Yes	5	1
								Yes	Not	5
				3	2	2	1		LTD	
				2	1	½	1			
				1	½	¼	1	No	x	1
				0	0	0	1			
	20	5		20	20	20	1	Yes	50	1
	15	15		15	5	3	1	Yes	15	2
	10	10		10	10	10	2	Yes	10	3
				10	8	5	1			
Printed Circulars or Inserts	10	5		10	5	5	1	Yes	LTD	1
	10	0		10	5	3	1	Yes	Not	2
	1	0		5	3	2	1		LTD	2
				3	3	3	1	No	x	1
				2	2	2	1			
				2	1	½	1			
				2	x	x	1			
				x	10	10	1			
				0	0	0	1			

Legend: "LTD". indicates there is a tolerance limit, but no definite figure was given.
"Not LTD." indicates there is no tolerance limit.
"x" indicates no data was given.

Why plastic packages sell more of everything, every day!

Transparent bandbox displays bath crystals as a gala gift!

How glamorous packaging can give unique sales appeal in a highly competitive market is once again dramatically demonstrated! Imaginative use of Monsanto Vuepak makes this kit of bath crystals all but irresistible!

Vuepak is the Monsanto tradename for cellulose acetate. The material is beautifully transparent so the nine individual containers get full display—and imprints colorfully with standard inks so the brand has elegant impact.

Package designers like to work with Vuepak because it forms at low cost into almost any desired shape. Further flexibility is gained because Vuepak combines so readily with cardboard or metal.

Small wonder Monsanto Vuepak is proving such a profitable packaging material for hundreds of drug and cosmetic items! In addition to its other qualities, it is light in weight to cut down shipping expense—yet has exceptional rigidity.

The package pictured is fabricated for Shulton, Inc., by the Union Specialty Co., 57 Main St., Bloomingdale, New Jersey.

Monsanto will gladly put you in touch with specialists in plastics packaging who will help you with your own container requirements. Write Monsanto Chemical Company, Plastics Division, Room 1236, Springfield 2, Mass.

Talk to Monsanto about packaging your products in

VUEPAK*

cellulose acetate

MONSANTO

Monsanto also supplies styrene and polyethylene for profitable packaging.

*VUEPAK: REG. U. S. PAT. OFF.

COSMETICS AND TOILETRIES

	Standard Items Repeat Orders Likely			Special Items Few Repeat Orders				Packaging Materials from Manufacturer's Stock		
	per cent limit on			per cent limit on overrun for				1. is nearest full case o.k.? 2. if yes, what per cent?		
	Over Run	Under Run	Number of Companies	5M-50M	50M-500M	Over 500M	Number of Companies	#1	#2	Number of Companies
	10	10	5	10	10	10	2	Yes	Not LTD	5
				10	10	5	1			
	10	5	1	10	5	5	1			
	10	0	1	10	5	3	1	Yes	10	5
Closures	5	10	1	10	x	x	1			
	5	5	2	5	5	5	2			
	5	0	2	2	1	1	1	Yes	5	1
	Not	LTD	1	1	1	½	1			
				0	0	0	3			
	10	10	3	10	10	10	2	Yes	Not LTD	5
	10	5	1	10	10	5	1			
	10	0	1	10	5	2	1			
Glass Containers	5	10	1	10	x	x	1	Yes	10	4
	5	5	2	5	5	5	1			
	5	0	1	5	3	3	1	Yes	5	2
	2	0	1	2	1	1	1			
	Not	LTD	1	1	1	½	1			
				0	0	0	4			
	10	10	8	10	10	10	4	Yes	Not LTD	1
				10	5	5	1	Yes	10	5
	10	0	1	10	5	3	1			
Folding Cartons	5	5	2	10	x	x	2			
	5	0	1	6	3	3	1	Yes	LTD	1
	3	0	1	5	5	5	1			
	Not	LTD	1	5	3	3	1			
	Not			1	1	½	1			
	LTD	10	1	0	0	0	2			
	10	10	5	10	10	10	2	Yes	10	4
				10	5	5	1			
	10	0	1	10	5	2	1			
	5	10	1	10	x	x	1			
Setup Boxes	5	5	4	5	5	5	2			
				5	x	x	2			
	2	2	1	1	1	1	1			
	1½	0	1	0	0	0	2			
	Not LTD	0	1							
	10	10	7	10	10	10	2	Yes	Not LTD	1
				10	10	x	1			
				10	5	5	1	Yes	10	5
Shipping Containers	10	0	1	10	x	x	2			
	5	5	5	5	5	5	2			
				3	2	2	1			
	5	0	1	2	1	1	1			
	2	0	1	2	1	x	1			
				1	1	½	1			
				0	0	0	2			
	20	0	1	20	x	x	1	Yes	Not LTD	1
	15	10	1	15	10	5	1			
	10	10	6	10	10	10	5	No	x	1
								Yes	10	3
	10	5	2							
Labels	10	0	1	10	10	5	1	Yes	x	1
	5	5	1	10	10	x	1			
	5	0	1	10	x	x	1			
	Not			10	5	2	1			
	LTD	10	1	5	5	5	1			
	Not	LTD	1	1	1	½	1			
				0	0	0	1			
	20	0	1	10	10	10	1	Yes	Not LTD	2
	10	10	1	10	x	x	1			
	5	5	3	5	5	5	1	No	x	2
Tape	0	10		5	x	x	1	Yes	x	1
	0	0	3	0	0	0	6	Yes	10	1
	0	x	2					Yes	2	1
	LTD	0	1							
	Not	LTD	1	LTD	LTD	LTD				
	10	10	3	10	10	10	1	Yes	15	1
	5	5	2	10	x	x	1	Yes	10	1
Adhesive	0	0	5	5	5	5	1	Yes	5	1
				0	0	0	5	Yes	Not LTD	3
	0	x	2							
								No	x	1
								Yes	x	1
	10	10	4	10	10	10	2	Yes	Not LTD	2
				10	5	5	1			
	10	5	1	10	x	x	1	No	x	1
Metal Containers	10	0	1	5	5	5	1	Yes	10	4
	5	5	2	1	1	½	1			
	5	0	1	0	0	0	3			
	2	2	1							
	10	10	6	10	10	10	5	No	x	1
								Yes	10	3
Printed Circulars or Inserts	10	0	1							
	5	5	1	10	10	x	1	Yes	5	1
	5	0	1	10	5	3	1			
	Not			10	5	2	1			
	LTD	2	1	10	x	x	1			
				5	5	5	1			

Legend: "LTD." indicates there is a tolerance limit, but no definite figure was given.
"Not LTD." indicates there is no tolerance limit.
"x" indicates no data was given.

SUPPLIERS OF PACKAGING MATERIALS

(Bags, Adhesive and Tape, Collapsible Tubes, Closures, Cans, Folding Boxes, Shipping Containers)

	Standard Items Repeat Orders Likely			Special Items Few Repeat Orders				Packaging Materials from Manufacturer's Stock		
	per cent limit on			per cent limit on overrun for				1. do you ship split cases? 2. do you ship nearest full cases?		
	Over Run	Under Run	Number of Companies	5M-50M	50M-500M	Over 500M	Number of Companies	#1	#2	Number of Companies
	10	10	2	20	10	5	1	No	Yes	3
Closures	5	5	2	10	10	10	2			
	5	0	1	5	5	5	3	Yes	No	1
	0	0	1					Yes	x	1
Glass Containers	x	x	x	x	x	x	x	x	x	x
	20	20	1	20	10	5	1	Yes	No	2
	20	x	1	15	10	10	1	No	Yes	3
	10	10	5	10	10	10	4			
Folding Cartons								Yes	Yes	1
	10	5	1	10	10	5	1			
	5	5	2	5	5	5	1			
	3	3	1	3	2	x	1			
				0	0	0	2			
	10	10	1	10	10	10	1	Yes	No	2
Set-up Boxes	5	5	1	5	5	5	1	No	Yes	1
	5	0	1	5	3	1	1			
	10	10	5	20	10	5	1	Yes	No	1
				10	10	10	2	No	yes	2
Shipping Containers	10	0	1	10	10	5	1			
	10	5	1	10	10	x	2			
	0	0	1	10	3	2	1			
	30	x	1	20	10	5	1	Yes	Yes	1
	10	10	2	10	10	10	2	No	Yes	1
Labels	10	0	1	5	5	5	1			
	5	5	2							
Tape	0	0	1	Not LTD	x	x	1	x	x	x
Adhesive	LTD	LTD	Nearest standard container 1	LTD	LTD	LTD	Nearest standard container 1	x	x	x
	5	5	2	20	10	5	1			
Metal Containers	5	0	1	10	10	10	3			
	0	0	1					x	x	x
				5	5	5	2			
Printed Circulars or Inserts	10	10	1					No	Yes	1
	10	0	1	x	x	x		Yes	Yes	1

SUPPLIERS OF PACKAGING MATERIALS

(Paper, Glass, Films and Foils, Cleansers.)

	10	5	2	15	10	5	1	Yes	No	1
	5	5	1	10	5	5	2	Yes	x	1
Closures								Yes	x	with extra charge 1
	10	10	2	15	10	5	1	No	Yes	1
Glass Containers	10	5	Plastic containers 1					Yes	x	with extra charge 1
	5	5	1							
	15	15	1	15	15	15	1	No	Yes	3
Folding	10	10	2	10	10	10	2			3
Cartons	10	5	1	10	10	5	1	Yes	x	1
	10	0	1	5	10	10	1			
	5	5	1							
	10	10	1	10	10	10	2	No	Yes	1
Set-up	10	5	1	10	5	2	1	Yes	x	1
Boxes	10	0	1	5	1	10	1			
	5	5	1							
	10	10	1	20	x	x	1	Yes	No	1
Shipping	7	0	1							
Containers	5	5	1							
	15	15	1	15	15	15	1	Yes	No	2
Labels	10	10	3	10	10	10	2	No	Yes	1
	5	5	1							
Tape	5	5	1	5	5	5	1	Yes	No	1
	0	0	2	0	0	0	1	No	Yes	1
Adhesive	0	0	1	x	x	x	x	x	x	x
Metal Containers	10	10	1	x	x	x	x	x	x	x
	5	5	1							
Printed Circulars or Inserts	15	15	1	15	15	15	1	No	Yes	1
	10	10	1	10	10	10	1			

Legend: "LTD." indicates there is a tolerance limit but no definite figure was given.
"Not LTD" indicates there is no tolerance limit.
"x" indicates no data was given.

ADD THE MAGIC OF GENUINE GOLD...

for packaging of enduring beauty

What better way is there to package quality products than to wrap them in the luxury of Hanovia Bright Gold.

The sparkling beauty and simple elegance of 22 Karat Bright Gold, applied economically by silk screen process, adds enchantment and charm to your packaging . . . adds new impact to your sales program.

And here's more magic: packaging beauty and distinction can be yours with Hanovia Bright Gold at a price comparable to common labeling. Durability, too, is another magical quality of this liquid gold. Fired on ACL, 22 Karat Bright Gold resists abrasion and solvents to provide packaging of truly enduring beauty.

Consult your glass supplier or glass decorator for quotations.

ENGELHARD INDUSTRIES

Hanovia

HANOVIA

CHEMICAL & MANUFACTURING COMPANY

1 West Central Avenue, East Newark, New Jersey

Beauticians Respond to Package Appeal

by Richard Gelb,

VICE PRESIDENT AND GENERAL MANAGER OF CLAIROL INCORPORATED

When we introduced our new "Come Alive Gray" hair rinses the response not only was highly gratifying in the beauty trade but caused a stir in a totally unexpected quarter—the packaging industry.

It wasn't simply the dramatic impact, sales appeal and tasteful modern design of the cartons in which we enclosed the bottles that caused excitement. Manufacturers of a huge variety of products employ effective packaging as a high-voltage merchandising aid today. What appeared to startle the packaging industry was that we had gone to such lengths to package a product intended primarily for use by professionals.

Beauticians, principally, would see the package; it was not a consumer product that would depend entirely for its success on meeting competition on store shelves. Why, then, they asked, didn't we avail ourselves of the more economical, if old-fashioned, method of shipping the bottles in plain, stencilled cartons?

Well, for twenty-five years we have been a beautician-oriented company. During that time we have found that beauticians are people, just like everyone else. They respond to an attractive package as much as any consumer. We reasoned that, having become accustomed to seeing fine packaging in the stores in which they trade, they would appreciate it on the shelves of their shops.

Moreover, we had a product with a new purpose. "Come Alive Gray" glamorizes gray hair of different shades, taking out any yellow discoloration and giving new life and beauty. No existing product did the job, we felt, and there was a genuine need for a product that would enhance the loveliness of white hair without disguising it. So that each shade of gray or white hair could be properly treated, we prepared "Come Alive Gray" in variations—"White Sapphire," "Silver Diamond" and "Black Pearl."

To underscore our belief that the product was an achievement in the hair coloring field, we decided to introduce it in a package of quality equal to the contents, even though, initially, it would be beauticians, chiefly, who would see it. *(Continued on page 134)*

The author, left, discusses the package and display carton of "Come Alive Gray" with Robert E. Jones, Clairol sales representative, center, and W. Taylor Bouchelle, vice-president in charge of sales of The Lord Baltimore Press, producers of the package.

New Perfection DROPPING PARTS

For Attractive Appearance . . .
. . . Perfect Performance

The New Perfection line of dropping parts is designed to meet your exacting demand for modern-looking units that function perfectly. We know that the user's satisfaction with your product may depend upon the reliability of the dropper—And, New Perfection dropping parts present your preparation at its very best.

The New Perfection reputation for excellence is maintained by use of the best quality materials, scrupulous attention to cleanliness and rigid inspection of all parts before delivery.

DROPPER GLASSES

are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

BULBS

are supplied in many styles and colors. Oil-Resisting AMEKINE synthetic rubber is used for oil preparations; natural rubber is supplied for other products.

CAPS

of plastic or metal, can be furnished in a complete range of sizes and colors.

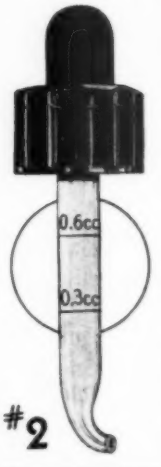
BOTTLES

in an attractive modernistic style in Amber, Blue, Green or Clear glass, are available, complete with dropping parts, in the following sizes: ⅛, ¼, ½, 1 and 2 oz.

DROPPER GLASSES CAN BE

CALIBRATED
IN COLOR

An inexpensive extra that adds great convenience to the use of your preparation. The dosage you desire in the color you specify is accurately and permanently printed on the dropper glass. Trade-marks and firm names can also be imprinted.



We Can Supply Dropping Parts To Fit Your Bottles or Furnish Complete With Our Own Bottles

Write for Samples and Quotations

PENNSYLVANIA GLASS PRODUCTS CO. INC.

"Glass Goods of the Better Kind"

430 N. Craig Street • Pittsburgh 13, Pa., U. S. A.

the search for beauty...

is your cosmetic package readily recognized?

does your cosmetic-ware invite new friends easily?

It is the job of all production wise Hazel-Atlas cosmetic-ware to win and keep customers.

It is all designed with a smart dressing table look that is welcomed in the home.

Beauty without, to suggest the beauty within.

There is an expert at your service at the nearest of the 32 H-A factories and sales offices.

HAZEL-ATLAS GLASS COMPANY *WHEELING, WEST VIRGINIA*

Packaging and Selling

Quality and Mass Distribution

Will automation and an increasing tendency to think in terms of mass distribution for American packaged products and an increasing dependency on heavy consumer advertising in marketing, decrease the quality of American goods? At least, if there is not a decrease in quality, with mass advertising and mass distribution, will there be a trend toward a uniform standardization which is substantially below the quality which could be achieved for that product?

Certainly, no conclusion can be taken here. In many fields, such as the automobile, household appliances, etc., there has certainly been no decrease in quality or performance within the price classification of the product. On the other hand, in packaged goods as in food products, chemical specialties, cosmetics, etc., it certainly can be said with emphasis that in a great many cases, there has been a provable quality decrease.

It is too bad that it is not polite in discussing things of this sort to mention specific products or specific company names. A really fascinating story could be written, if case histories were specifically delineated with product and company names, showing just how this has happened and what has taken place.

The industries that we have mentioned above contain numerous case histories in which large companies have purchased dynamic, growing, small companies, where the dynamic growth has been based primarily on a superb quality and product performance. By the time the big company got through reorganizing the newly acquired company, the purchasing department and cost department of the big company had reduced the newly acquired product to a standard of acceptable mediocrity. Of course, it could be said that the big company possibly adjusted this new product to a mass market acceptance, and to a cost basis for this market.

Again, a frank case history discussion with names would mention companies and products which have declined from a dominant position entirely and exclusively because of a cynical management attitude toward product quality. Many of these case histories are every day knowledge to members of the industry. For instance, not too long ago, one of the leading perfume companies in this country, at one time an outstanding success and with a long and remarkable record of company performance was sold on the auction block for a price that cost a little bit more than the real estate and the inventory of the product. The man who was directing this company considered himself a wonderful salesman, and, incidentally, was rated as a very lavish entertainer. This man always thought that the key things which counted in business were salesmanship, entertaining, advertising and gimmick packaging. He was notorious among the supply people, particularly those supplying perfume materials, as one of the sharpest buyers in the trade who continually drove a hard bargain for cheaper and cheaper materials.

Parallel to the decline and fall of this perfume company, there is another perfume company which has made one of the finest records of business growth, stability and profits in the entire history of the perfume business. The management of this company takes a rather different viewpoint in that they put in a very secondary position all of those things, such as mass merchandising, gimmick packaging, advertising and lavish entertainment, which distinguished the first company. This second perfume company has a rather extraordinary purchasing policy of always seeking the highest quality merchandise, with price as a secondary factor, even though these materials go primarily into a moderate priced cologne. This particular company continually has been under investigation by other members of the industry who cannot fathom or will not accept the fact that this company is so outstandingly successful while still ignoring the orthodox methods of advertising and selling. Other industry members are insistent that there is some hidden element, which, if they could only ferret out, would make, them too, equally successful.

There are times when there is nothing so astounding as the truth. Apparently, there are also times, in this miracle age of exuberant selling and advertising, when it is equally astounding to many business men that a product will grow and sell on its own momentum solely because it is a product of superb quality.

It just doesn't seem possible today to prove that among all the things which make a product continue to move over the counter into the public's homes, which would include selling, advertising, entertaining, store display, gimmicks, gadgets, premiums and trading stamps, that the one little incident of product quality could play such an important part.

Tougher Super

As we have repeatedly stated in this column, a lot of folks in this trade who are turning to supermarket distribution are not yet fully aware how swift the pace will be.

That this pace will grow faster and faster is shown by the hardening attitude in some supermarkets for

the rate of turn over on the drug and cosmetic shelf.

It is shown more clearly by the way in which supermarkets are quietly expanding with almost every conceivable kind of non-food product sold through any kind of a retail outlet.

This new competition which includes such moves as a new department by the A & P for magazines, another super group with cut flowers and plants and still another, that is Grand Union, with Hi-Fi records. This provides some indication of the strenuous fight within the non-food industries not only for floor space but for location of display.

The Sound and the Fury

How economic is the kind of savage competition that shoulders its way into an industry or a product market with the lavish and overwhelming employment of capital in advertising and promotion?

This is a situation in which this trade is familiar, particularly in such things as tooth paste and lipsticks.

It is probably true that this kind of competition will increase as the television audience becomes universal and as self service makes retailing an automatic machine.

Very often, these vigorous selling attacks upon a market are not made because a superior product has been discovered or because the market has not reached the saturation point but simply because some large company wants to expand further and is able to employ large capital for that purpose.

According to a recent article in "The Wall Street Journal," Europe, that area of low pressure selling, dignity and restraint in promotion and canny consumer shopping is about to be subjected to this new era of American marketing. As an example, here is a quote from that report: "A few days ago, about 50 weird little Messerschmidt motor scooters, with enormous Gleam tooth paste packages mounted above their roofs, converged on Piccadilly Circus from the London suburbs. Each had a loud speaker announcing the news that P & G was introducing a dentifrice to the British markets; uniformed Gleem girls handed out samples to throngs of office workers. Within a few days, free packets were handed out to every householder in southern England; some got three or four tubes. This is a challenge both to the top-selling Unilever tooth pastes—Gibbs, Pepsodent, Mentasol—and to the well-established Colgate paste."

England has a lot of other tooth pastes, and I imagine they need another one about as much as they need another Cyprus.

Gleem entered the United States market with an assault that has seldom been equalled in merchandising fury. Reports rumored a sampling campaign running into many millions of homes sampled and an advertising campaign said to reach as much as $18,000,000 in a relatively few months. The pressure upon the retailer as well as upon the consumer was enormous and concentrated.

We may say that this is private enterprise at its best but we must also guess that it is private enterprise which can only be employed by a very few in any one industry.

Packaging Success Story

Everybody takes pills, according to the Richford Corporation, and thereby hangs the tale of one of the cutest and most attractive packages of this year and one of the real packaging success stories. Richford further declares: "Yes, sir, everybody takes pills . . . pink pills, white pills, cerise pills, yellow pills, big pills, little pills, square pills, round pills, stay-awake pills, go-to-sleep pills, vitamins, saccharin!!! People are either overweight or underweight, they have headaches, backaches, toothaches, and sacroiliacs. From January 1st to December 31st, they take pills around the clock!!!"

Richford's new pill boxes are individually and smartly boxed in black and gold, with a selection of intriguing designs and phrases.

Paying Advertising Agents

That ancient method of compensating advertising agencies may be due to some degree of adjustment. The anti-trust consent decree recently concluded with the Justice Department over the method of advertising agencies' compensation has things boiling.

Mr. Gamble of the American Association of Advertising Agencies said recently in a statement that he didn't think there was any reason for any particular drastic action changing the method of compensation.

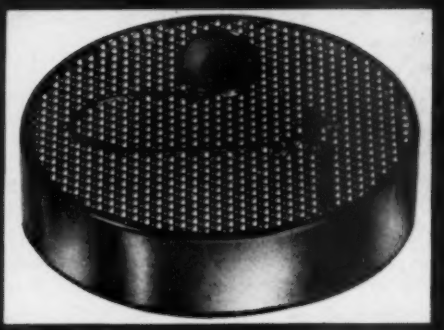
The method of agency compensation today, that is 15 per cent of the cost of media is as outdated as the one horse shay and is very specifically unfair to large groups of media and to many advertisers. Fifty years ago, when there was a good reason for a wholesaler of advertising space, this method worked pretty well. Today, the publisher is not compensating the advertising agency for any effort in selling nor does the agency or the advertiser consider this compensation is pay for any sales activity on the part of the agency.

From the viewpoint of the advertiser, it is totally unfair for an advertising agency to receive the same

and now the NEW Gem-cut

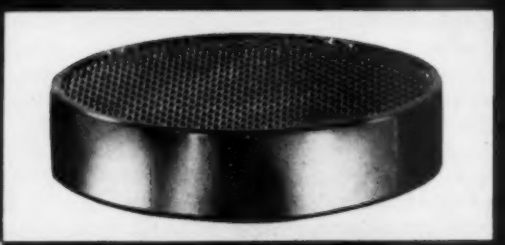
GOLDCOTE PLASTIC CAPS WITH INLAID BASKET WEAVE DESIGN

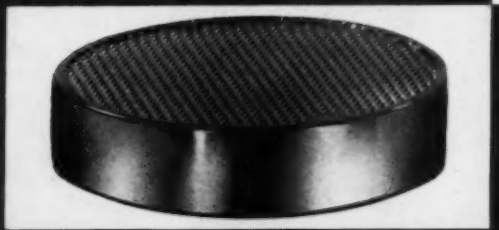
luxurious additions to RICHFORD'S complete line of Closures for Bottles and jars —*at no increase in price over plain caps.*

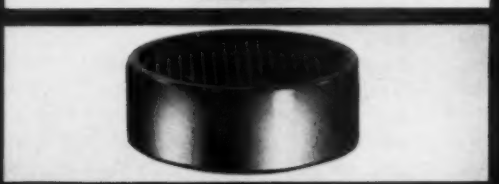


Glittering, gem-like, these new caps add value to your product — transform plain bottles or jars into products of beauty.

And on special order, you may obtain them with your crest, trademark or special art work added. Sizes presently ready for 33 mm and 58 mm necks.







Packaging experts have called them the most exciting new caps in years — write now for samples and prices.

RICHFORD
CORPORATION
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total remuneration for a page in "Life" or the" Ladies' Home Journal" that he would receive from expending the same money in eight or 10 separate publications, including one or two trade magazines. This would be even more drastically true if the advertising agency changed the copy or art work for certain kinds of magazines as an adjustment for a particular type of reader audience.

No matter what some advertising agency men may say, there has been a conscious or unconscious drive towards the magazines with a million or more circulation, and a turning away from the smaller, specialized circulations.

This method of compensation has been specifically and drastically unfavorable toward developing a true agency interest in point of sales advertising, particularly with reference to trade magazine advertising.

The quicker the big advertisers insist on paying agencies on the basis of work actually performed, exactly as an accounting firm or a legal firm is paid, the better it would be for all advertising. We cannot see any obstacles that cannot be overcome if an agency submit a basic estimate of the cost of services at the time the budgets are submitted for planned seasonal advertising or planned advertising campaigns.

It is about time the advertising profession recognized the plain fact that there is more than one way to spend a million dollars for advertising and that each way has its varying costs.

Emancipation Proclamation

Probably the most dangerous competitive jungle in America today is the grocery supermarket. These people have pyramided a dynamic growth to a point where it seems that they must stifle each other to determine the survivors.

This competitive jungle has been fostered and built up as much by some of the food manufacturers as by the supermarkets.

While the supermarket has been sponsoring the disastrous war now being waged in the trading stamp field and by extravagant demands on the manufacturer for more concessions by using their potent weapon of preferred display space, the manufacturer in turn has been loading the market with gimmicks, gadgets, premiums and other silly and extravagant deals.

Because of this situation, it is more than interesting to see one leading food producer, that is Ralston Purina, make a declaration of emancipation from this stifling competitive mess.

In a recent advertisement in grocery trade magazines, Ralston declares, "GROCERS OF AMERICA, REJOICE! NO MORE CEREAL PREMIUMS! Ralston Emancipates the Market from Litter, Twitter, Clitter, Clatter, Pilfer and Piffle."

Ralston then goes on to declare that the American grocer has endured cereal premiums for years, that they have cluttered his shelves, littered his displays, and stifled his stocks. "He has been menaced by rocket guns, space ships, dinosaurs and derringers. He has had his mind muddled by deals, dickers and dime store donations."

Ralston then declares that in the future they have nothing to sell except "only delicious cereal from the top to the bottom of every package of Wheat-Chex, Rice-Chex, Instant Ralston and Regular Ralston."

As an agitated and sorrowful observer of what is happening in American marketing, I urge every reader to purchase and enjoy Ralston cereal.

Self Competition

One of the favorite subjects of this column has been the great increase of self competition among leading manufacturers and results of this growth in self competition. Now we hear that some trouble is developing in the cigarette industry, which certainly has been one of the leaders in self competition. The cigarette companies have not only aggressively featured multiple brands but also within each of these brands they have had the regular size, the king size, the filter tip and now they are thinking of adding a duplicate package, that is the hard box package. We hear that some of the large retailers and chain stores are rebelling at this successive duplication and refusing to carry both regular and king size in one brand, and we also hear that this duplication is becoming a serious problem of survival for fringe brands.

If this momentum for self competition continues, so that the big companies feel compelled to enter into every area and every section of the market, not only with brand duplication but with variations of these brands, then we must certainly look forward to a new phase developing in the theory of monopoly.

Scrambled Merchandizing

Most observers looking at the business scene today are apt to feel that we have reached a high degree of "scrambled" merchandising in which there is a general tendency for almost everyone to crowd over into other people's home grounds. This has been very noticeable in some branches of retailing as with the grocery supermarket, and it has been a particular problem of some branches of this industry.

Now, we hear that a leading retailing expert, Malcolm P. McNair of the School of Business Administration, Harvard University, believes that this will even be accelerated.

In a recent talk Professor McNair stated that "as a result of the war time expansion of industrial facilities a likely consequence will be much more "scrambled" merchandising, in which everybody is in everybody else's business, and a continued breaking down of the conventional channels of retail distribution. This may be called a management revolution which tends to the view that good management can do most anything."

Retail Automation

The grocery supermarkets are turning to automation in retailing, such as it is, more than any other retailers. Probably for this reason, these folks like to let their imagination roam. One of these retailers felt quite sure that the future grocery store would display a battery of vending machines, as an extension

We can supply fine quality handmade glass containers made to private mold specifications or in a stock design such as the one illustrated. They can be furnished plain or with fired-on ceramic labels.

CARR-LOWREY GLASS CO.

Designers and manufacturers of fine glass containers

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of the store, which would operate 24 hours a day for various food staples.

This particular executive thinks that the future of food store retailers will be greatly linked with IBM cards which the retailers will distribute to all regular and perspective customers. These cards will have various colors for food classifications, and preceding her shopping trip, the customer will simply punch these cards with the various items she wants. The customer will then take the punched cards to the store where they will be processed, the order assembled and ready to check out in about five minutes.

Far be it from us to disparage these flights of the imagination. We feel quite sure however that no form of automation will ever interfere with the pleasure of shopping.

Advice from Canners

Food Canners have been more and more concerned about the way they have been pushed around in food supermarkets in regard to space for stock and position within the store. The Canners have found that there has been an increasing tendency to push the display of canned foods nearer and nearer to the rear of the store and to a less desirable position from the viewpoint of impulse buying. With the advent of frozen foods, this further threat has brought the canning people together with an increasing awareness of their need for more modern marketing techniques.

At a recent meeting of the Tri-State Packers Association, the Canners had some advise along this line that is certainly applicable to the market for any kind of packaged product.

Here are the suggestions of a food wholesaler as a way to strengthen manufacturer—wholesaler—retailer patterns. He suggested:

1. Cartons should be packed to meet the needs of suppliers, to avoid the need to buy broken case lots.
2. Goods must arrive in good shape for shelf display and the packers themselves should absorb in their "swell allowances" any loss on damaged merchandise.
3. Products must be priced competitively.
4. Packers should share with retailers and wholesalers the cost of advertising from a retail sales appeal standpoint.

More specific were the suggestions of an executive of one of the large supermarket chains. His suggestions were:

1. A realistic price policy is necessary to assure "Shelf velocity."
2. Labels must be immediately eye catching, the customer doesn't linger for a second look.
3. Product quality must be uniformly excellent at all times.
4. Rapid and efficient delivery service can help the retailer meet his warehouse and shelf problems.

Notes and Comments

One of the important reasons for continuous advertising in this country is the great fluidity of the American market. Americans just don't like to stay put. According to recent figures, one in six of every American moves each year, or to be more exact, nearly 25,000,000 Americans move to new homes each year.

It looks as if the fashion for diversification in business is pretty well running its course. Whether this is the normal cycle of enthusiasm so characteristic of this country or whether it's the first sign of cold feet is anyone's guess. Anyhow, we are beginning to see in the financial news quite a few "Spin-Offs."

The consumer analysis studies made by a number of leading newspapers in this country have always been a source of very valuable factual data to us. The new ones for this year are just beginning to come in and we have received the consumer analysis of "The Seattle Times" and also that of the McClatchy newspapers, that is "The Sacramento Bee," "The Fresno Bee" and "The Modesto Bee." As usual, in these consumer studies, we note some interesting changes in brand positions and also some very interesting sales trends.

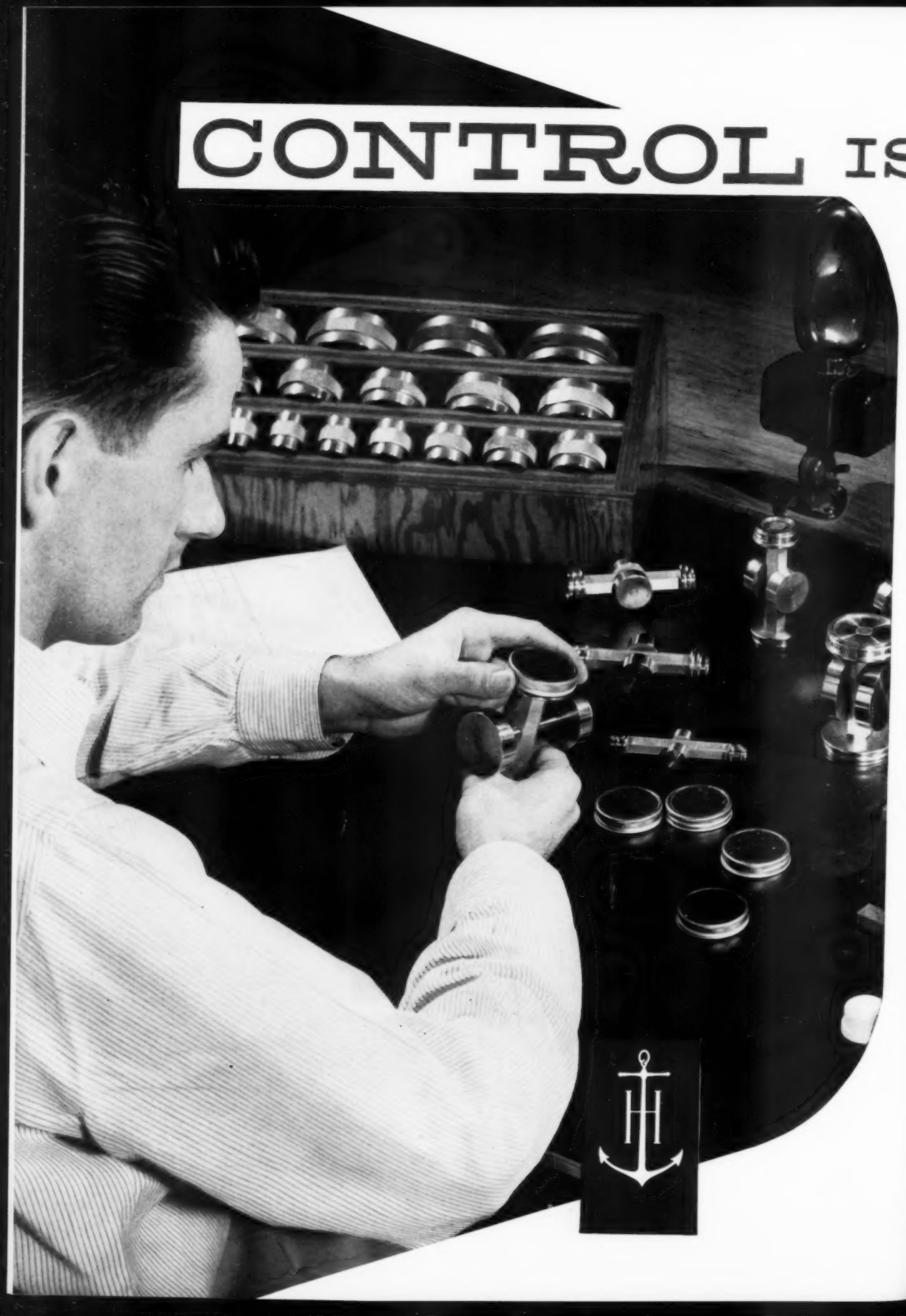
The grocery stores continue to get an increasing proportion of this industry's sales. In Seattle, 56.5 per cent of the people are now buying some toilet article in the grocery store, with the grocery stores getting 13.7 per cent of the industry's business in this city market. All other stores, that is department, independent drug, chain drug and variety stores, showed a slight loss in consumer's favor, with house to house sales now at 6.5 per cent, a moderate increase.

In the three "Bee" cities, the percentage favoring the grocery store for certain toilet articles is considerably greater than Seattle, that is running for the three cities, 64.1 per cent, 67.5 per cent and 72.5 per cent for each of the three cities.

When it comes to a contest, this industry is a pretty good winner. Some time ago, we reported Breck as the winner of the Flower Association award for the best use of flowers in advertising. We then reported quite a considerable number of this industry's companies who achieved the high distinction of an award from the Paper Match Association, and now we have the pleasure to announce that Helena Rubinstein has just received the award bestowed by the American Music Conference "for the most effective use of music as a theme in advertising of non-musical products." The product—Jazz Lipstick.

The F. W. Woolworth Company has been vigorously converting stores into self service. By the end of the current year, the company expects to have 650 of its 2,064 units in self service operation.

Flav-R Straws, Inc. is marketing an intriguing new idea. This is a straw with a "built-in" flavor. The flavor is hidden in the straw's filter. All you have to do is to dip one of the straws in milk, wait a minute for the milk to moisten the filter and then sip. As the milk passes through the filter, it picks up the flavor. This sounds to us like a radical new idea for dispending. Why not a straw with built-in castor oil?


CONTROL IS

NEWS IN PACKAGING...

Continental May Merge with Gair, Hazel-Atlas; Buys Canadian Firm

A proposed merger of Continental Can Company, Inc. and Hazel-Atlas Glass Company, approved by directors of both companies, awaits the decision of Hazel-Atlas stockholders, who will vote on the plan at a special meeting scheduled to be held within a few weeks.

Terms of the proposal provide for shareholders of Hazel-Atlas to receive 999,141 shares of Continental Can common stock, which means a 46/100 share of Continental for one share of Hazel-Atlas. On this basis Continental would have a capitalization of $79,648,000 long-term debt, 150,000 shares of $3.75 cumulative preferred stock, and 8,755,499 shares of common stock. Hazel-Atlas' present capitalization consists of 2,172,045 shares of common stock.

At 1955 year-end, Hazel-Atlas had total assets of $37,884,425 and working capital of $19,904,256. Continental's figures were $381,917,101 and $110,815,816.

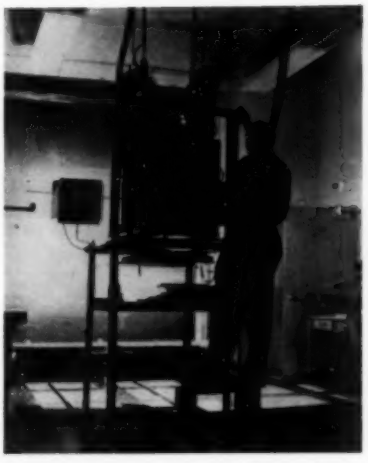
General Lucius D. Clay, chairman of the board of Continental, and George E. Dyke, chairman of the board of Robert Gair Company, Inc., have announced that they agree in principle on a basis for the merger of the two enterprises, subject to the usual checks of all business and legal matters. The merger has been approved by the directors of Continental and the executive committee of Robert Gair, both of whom will recommend it to their stockholders.

The proposal calls for an exchange of common stock at the ratio of 8/10 share of Continental for each share of Gair. Holders of Robert Gair convertible preferred would receive shares of a new convertible preferred issue of Continental, share for share. Each share of the new issue would be convertible into 2.4 shares of Continental common stock.

Continental has acquired Canadian Crown Cork Co. Limited. The announcement was made jointly in Montreal by Frank A. Whittall, president of Continental Can Company of Canada Limited and John M. Gardiner, president and general manager of Canadian Crown.

R. F. Elder Is Plax President

Robert F. Elder, previously executive vice-president, has been elected president of Plax Corp., Hartford, Conn., plastic container, sheet and film manufacturer.



This giant copy camera is part of the extensive photographic and reproducing equipment available in Continental Can Company's new $7 million laboratory for research and engineering in Chicago. Machine drawings are photographed and reproduced on cloth for use by engineers and shops in manufacturing parts and equipment. By the end of the year, 600 people, about half of them scientists and engineers, will work in the laboratory developing new containers, new machinery to make and close the containers, and new products for packaging in metal and related materials.

Head MCA Packaging Group

P. W. Tucker, Phillips Petroleum Company, Bartlesville, Okla., and J. O. Browning, Merck & Co., Inc., Rahway, N. J. have been elected co-chairmen of the chemical packaging committee of the Manufacturing Chemists' Association.

Designers Claire McCanna and Marjory Markley, attending Consolidated Lithographing Corporation's Forum for Package Designers, stop to examine a sheet of Avon's "To a Wild Rose," which has just come off the press. Misses McCanna and Markley have both done designing work for Avon products. On the left is Maryan Linck, publicist for Consolidated.

Seamless Capsule in Production

A one-piece seamless capsule, being produced by a new thermoplastic process, has been announced by the General Capsule Corp., Fraser, Mich. One production unit is in operation and others are being built. A first-year production rate of more than seven million of the thermoplastic bubbles per week is the goal of the company's expansion plans.

Drug, Cosmetic Tube Demand Up

Shipments of collapsible metal tubes for pharmaceuticals and toiletries totaled 78,095,600 units in April, an eight per cent increase over April, 1955, according to a report from the Collapsible Tube Manufacturers Council.

For the first four months of 1956, the council states, shipments amounted to 351,557,424 units, 39.4 per cent above last year's comparable period. The demand by dentifrices and pharmaceuticals continues strong, according to Lester B. Platt, executive secretary of the council.

Henri Colonna Visits U. S.

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On Packaging Inst. Board

Frank W. Cray, vice-president, International Printing Ink Division of Interchemical Corporation, has been elected to the Packaging Institute board of directors.

Mr. Gray has been chairman of the technical committee of the National Association of Printing Ink Makers, served on the standardization of process colors committee of the Printing Institute of America and received a rarely given Packaging Institute Scroll Award for his chairmanship of the "Know Your Printing Processes for Packaging" seminar at the Institute's 16th Annual Forum.

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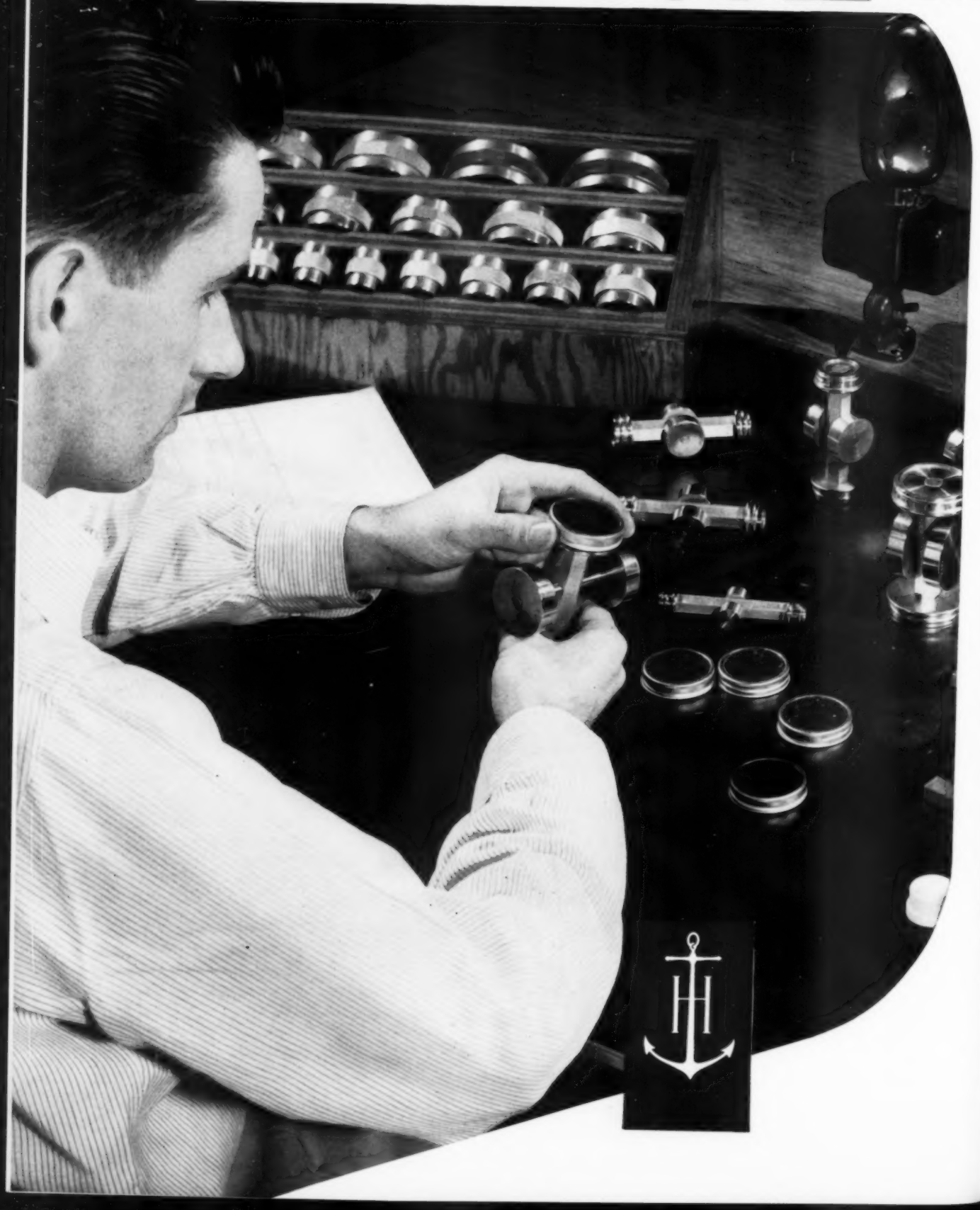

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To prevent shattered glass, Shulton has packaged its two new spray colognes, Escapade and Desert Flower, in plastic-dipped bottles. Escapade is decorated in bright pink and Desert Flower in gold and white. Both are capped in gold.

Package Design Exhibit

Information about the Third American Package Design Exhibition and Awards Competition, sponsored by the Package Designers Council, has been announced. Deadline for entries, which may be submitted by designers, product manufacturers, packaging suppliers, and advertising agencies in the United States and Canada, is Nov. 1. Results will be announced early in 1957. Official entry forms will be distributed about September 1.

A new feature of the 1956 competition will be a cash award of $1,000, donated to the Council by the Aluminum Company of America, for presentation to the designer of the package that best illustrates effective application of aluminum foil. The designer of the most outstanding entry in the exhibition will receive the Irwin D. Wolf Award.

In addition, awards will be presented to designers of top-ranking packages in twenty-one categories, and certificates of recognition will be given product manufacturers and packaging suppliers responsible for all award-winning packages. All packages in the exhibition will be on public view early in 1957.

Further information about the exhibition and competition is available through the Package Designers Council, 12 East 46th Street, New York.

Gair Safety Supervisor

William Atkinson Jr. has been appointed safety supervisor of plant operations for Robert Gair Company, Inc., George B. Greenwood, vice-president in charge of industrial relations, has announced.

Novel Type Face for Atarax

The package and label for Atarax, J. B. Roerig and Company's tranquilizer, carry the name of the product spelled out in letters that look like Greek capitals. The type face is meant to be an active reminder of the Greek word "ataraktos," meaning "freedom from confusion, peace of mind," and which supplied the name and slogan for the Pfizer drug.

But the type is not Greek. Called Weiss Bold, it is one of seven related faces designed between 1928 and 1930 in Germany by the late Prof. E. R. Weiss.

Sun Tube Div. Employment Mgr.

A. Holland Fairchild, previously assigned to Sun Tube Corporation's production and sales departments, has been appointed employment manager of the company's Sunnex Division, according to an announcement by Kenneth M. Leghorn, president of Sun Tube.

KARL W. MUELLER

Crown Cork & Seal Vice-Pres.

Karl W. Mueller has been named vice-president and director of manufacturing of Crown Cork & Seal Company, Inc., according to Russell Gowans, president. Mr. Mueller will be responsible for directing and coordinating manufacturing operations of the company's thirteen plants throughout the U. S.

Kellman Forms Printing Company

Sidney Kellman, former sales manager of the Pantone Press, Inc., has organized the Chroma Printing Corporation, 480 Canal Street, New York 13, according to an announcement. The company will design and produce packaging folders, counter cards, booklets, inserts, and other merchandising materials for the drug and cosmetic industry.

Owens-Illinois Constructing Bottle Mnfg. Plant in Cuba

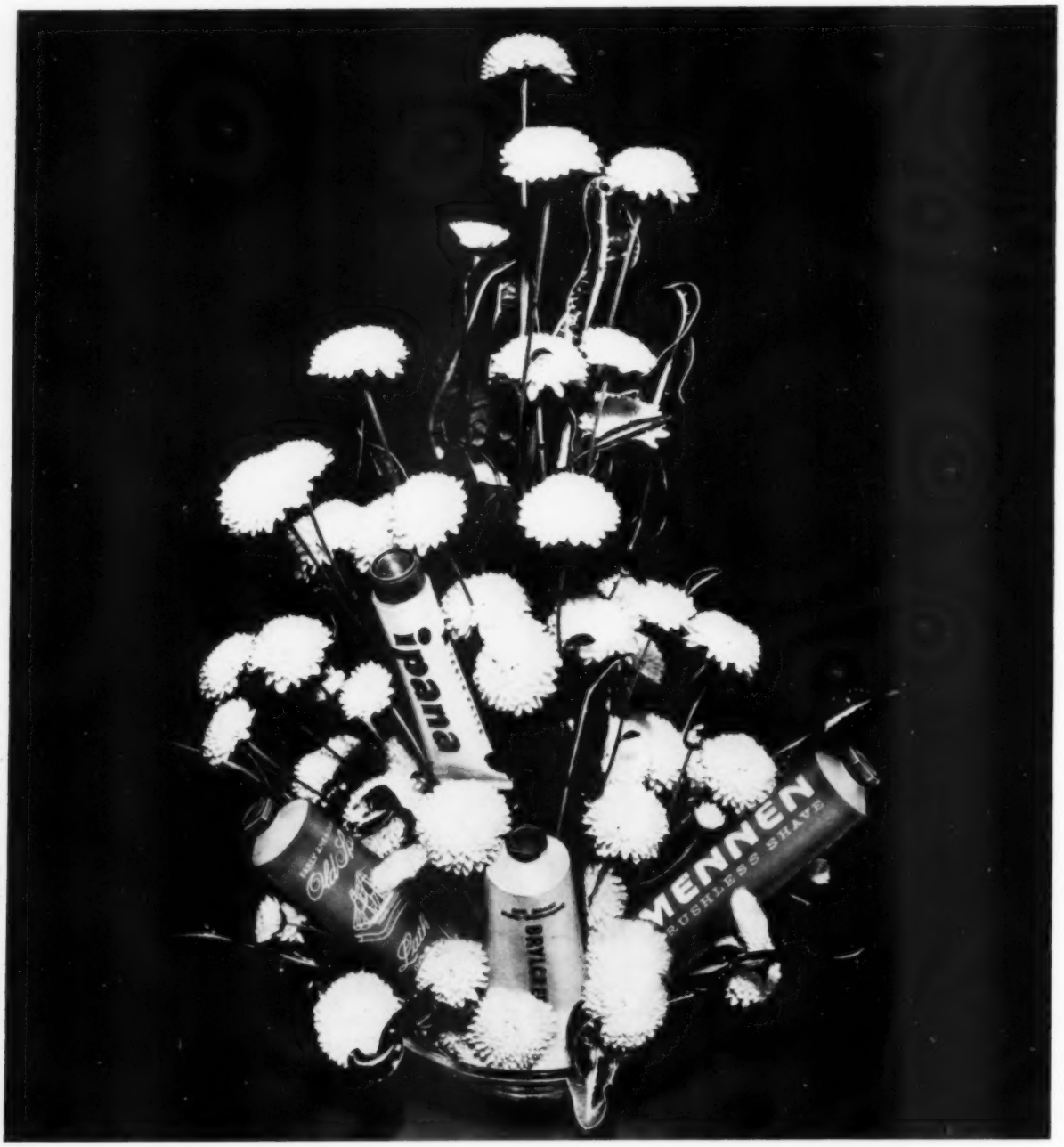
Owens-Illinois Glass Co. has begun construction of a multi-million dollar bottle manufacturing plant at San Jose de las Lajas, twenty miles southeast of Havana. Government and business officials from Cuba and the United States attended ground-breaking ceremonies June 15. The 148-acre site is on the Central Highway and the Occidental Railway about a mile south of San Jose de las Lajas.

Scheduled for completion in the latter part of next year, the plant, equipped with three glass melting furnaces, will be capable of producing about 72 million bottles and drinking glasses each year. Principal products will be glass containers for packaging of drugs, beverages and foods. The plant will employ about 200, all Cubans except for a few essential technicians to be drawn from the company's production staff in the United States. It will be one of the most modern and completely integrated of O-I's 31 plants.

Gair Promotes Oechsle

George A. Oechsle Jr. has been appointed assistant manager of the American Coating Mills Division, Elkhart, Ind., of Robert Gair Company, Inc., Norman F. Greenway, senior vice-president in charge of folding carton operations, has announced. With Gair since 1946, Mr. Oechsle has been superintendent of the Gair Cartons Division, Piermont, N. Y.

The newly styled corrugated shippers being used by A. H. Robins Company, Richmond, help assure safe shipment of prescription drugs. A series of interior packing pieces form cells separating the bottles, and four additional packing pieces surround the bottle cells, providing an extra thickness of corrugated board as a cushion against shock. The imprint on one end of the shipper is designed to provide correct identification of shipper and contents and has a standardized space for labelling.



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Cincinnati 8, Ohio: Ralph H. Auch, 3449 Custer Road.
New Orleans 19, Louisiana: R. P. Anderson Co., 925 N. Solomon Pl.
Houston 6, Texas: R. P. Anderson Co., 514 West Main St.
Dallas 19, Texas: R. P. Anderson Co., 2503 West Mockingbird Lane
West Coast: Wm. J. Stoepker, 301 E. Colorado, Arcadia, California
Canada: Sun Tube Corp., 145 Spruce Street, Ottawa, Ontario
Mexico: Tubos de Estano, S. A. de C. V., 174 Oriente No. 267, Colonia Montezuma, Mexico, D.F.

Patent THOUGHTS AND TRENDS

by Thomas Cifelli, Jr
PATENT ATTORNEY*

HALOGENATED PHENOLS AND DEXTRAN IN PATENT NEWS

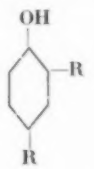
Chlorinated Phenols

Four patents of general interest dealing with chlorinated phenols or derivatives were issued since the last appearance of this publication. They will be considered in numerical order.

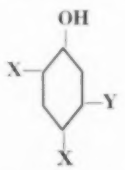
U. S. 2,745,881 was issued to The Dow Chemical Company on an improved method for making asymmetrical bis-phenols.

According to the patent, the conventional method of making these phenols by reacting a halogenated alkyl phenol and an halogenated saligenin-type compound in the presence of an acid condensing agent such as sulphuric acids gives poor yields and is impractical for commercial use because of the time required.

According to the invention, asymmetrical halogenated alkyl bisphenols are formed in a two-step process comprising the chloromethylation of a compound of the general formula:



wherein one R is an alkyl group of one to four carbon atoms and the other R is one of the halogens chlorine and bromine, and the subsequent condensation of the chloromethylated alkyl halo phenol with a 2,4- or 2,4,5-halogenated phenol having the general formula:



wherein each X is chlorine or bromine and R is chlorine, bromine or hydrogen, in the presence of a catalytic amount of an aluminum halide.

*Richards and Cifelli, Newark, New Jersey.

The following example taken from the patent illustrates the details observed in carrying out the process.

> 170.5 grams of 4-chloro-2-isopropylphenol, 92.4 grams of 40 per cent aqueous formaldehyde and 590 grams of concentrated hydrochloric acid were mixed together in a vessel and mechanically stirred. The mixture was heated at 45° to 50° C. with stirring for twelve hours with a slow stream of hydrogen chloride bubbling through the mixture. Reaction appeared to be complete after the first two hours of heating. The mixture was cooled and 326 grams of tetrachloroethylene added with initial stirring. After the two layers separated, the lower organic layer was washed and dried. The tetrachloroethylene solution of chloromethylated phenol was added dropwise over the course of two hours to 118.5 grams of 2,4,5-trichlorophenol in 204 grams of tetrachloroethylene mixed together with 10.6 grams of anhydrous aluminum chloride at a temperature of 90° C. The stirred mixture was maintained at a temperature of 90° to 95° C. during the addition. During the following half-hour period of heating, substantially no hydrogen chloride vapors could be observed. The reaction mixture was then cooled and to this was added a mixture of concentrated hydrochloric acid and ice to dissolve the aluminum chloride. After separation of the two layers, the lower organic layer was washed with water and then dried. On cooling the organic layer the bisphenolic product separated out. This was filtered and dried to yield 57 per cent by weight of 3′,4,4′,6′-tetrachloro-6-isopropyl-2,2′-methylenediphenol based on the initial 2-isopropyl-4-chlorophenol. The bisphenolic product had a melting point of 183° to 186° C.

Another method patent dealing with the purification of 2,4,5-trichlorophenol was issued to Olin Mathieson Chemical Corporation as U. S. patent 2,748,174.

The inventors, Jenney and Nicolaisen, point to the fact that in making 2,4,5-trichlorophenol from 1,2,4,5-tetrachlorobenzene a number of contaminants are formed. Methanol which may be used as a solvent for the hydrolysis reaction tends to cause some production of trichloroanisole and dichlorodimethoxybenzene. Also, the presence of the usual small amounts of other tetrachlorobenzene isomers causes the production of undesired position isomers of 2,4,5-trichlorophenol.

The inventors also note that there exists a substantial demand for a high purity 2,4,5, - trichlorophenol product (doubtless referring to its use in making hexachlorophene) and that the demand is for a product having a melting point over 65° C. and a color from white to near white in the molten state. Also, the product should be at least 99 per cent pure.

The trick hit upon by the inventors involves employing a step-wise neutralization process in recovering 2,4,5-trichlorophenol from the caustic hydrolysis products.

In the words of the inventors:

> The process of our invention thus essentially requires neutralizing crude 2,4,5-trichlorophenate solution by addition of mineral acid thereto in an amount sufficient to neutralize excess alkalinity of the solution and a minor proportion of the phenates present. The neutralized phenates are released as the free phenols which separate from the dilute aqueous mixture as a separate phase, i. e. when the total phenate-phenol concentration is not more than about 10 per cent by weight. Thus, we contemplate the addition of water, when required, to adjust the phenate-phenol concentration to not more than 10 per cent by weight, either prior to the first neutralization step or immediately thereafter, whereby the resulting

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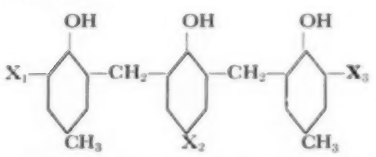
phenols are phased out then and may be separated from the aqueous phase which contains the remaining unneutralized phenates.

The aqueous phenate phase separated from the phenol phase is further neutralized by the addition of mineral acid but in an amount sufficient only for recovery as the free phenols of substantially less than the total of the phenates remaining in solution. The phenols phase out upon the second neutralization step without further adjustment of phenate concentration, and are separated from the aqueous phenate phase and recovered as the desired pure 2,4,5-trichlorophenol product.

The inventors also recommend a pretreatment of the 2,4,5-trichlorophenate by steam distillation to remove some of the caustic and soluble impurities, as it lowers the required amount of acid for the first step of the neutralization and permits a greater amount of acid to be employed in the second neutralization step, the claim being that highly increased yields of the high purity products result thereby.

Monsanto obtained a patent (U. S. 2,749,314) on the invention of Beaver, Shumard and Stoffel of new halogenated tris-phenols. The new compounds are said to have exceptional antiseptic properties in cosmetic formulations and detergent compositions.

The new compounds have the general formula



where X_1, X_2 and X_3 are like or unlike halogen atoms, and their corresponding alkali metal salts.

The preferred tris-phenols are 4 - chloro - α,α' - bis(2 - hydroxy - 3 - chloro - 5 - methylphenyl) - 2,6 - xylenol; 4 - bromo - α,α' - bis(2 - hydroxy - 3 - chloro - 5 - methyl - phenyl)-2,6-xylenol.

The degree of growth of Staphylococcus aureus in compositions containing 4 - chloro - α,α' - bis(2 - hydroxy - 3 - chloro - 5 - methylphenyl) - 2,6 - xylenol and analogous halogenated trisphenols was determined by incorporating the tris-phenols in an "Ivory" brand white high grade soap to form two per cent by weight compositions. Aliquots of each were then added to a neutrient agar so as to give concentrations of 1.25 p.p.m., 5 p.p.m., and 10 p.p.m. The agar was poured into a petri dish, allowed to harden and then streaked with a 24 hours old culture of S. aureus. The incubation was for 72 hours at 37° C. and the degree of growth as given in the patent follows:

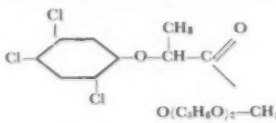
Halogenated Tris-Phenol	10 p.p.m.	5 p.p.m.	1.25 p.p.m.
4-chloro-a,a'-bis(2-hydroxy-3-chloro-5-methylphenyl)-2,6-xylenol	—	½+	+
4-chloro-a,a'-bis(2-hydroxy-3-chloro-5-tert. butyl-phenyl)-2,6-xylenol	+++	+++	0
4-chloro-a,a'-bis(3-chloro-4-hydroxyphenyl)-2,6-xylenol	½+	+++	+++

Legend:
— No growth.
½ + Extremely light growth.
+ Very light growth.
++ Light to moderate growth.
+++ Normal heavy growth.
0 Not tested.

Dow Chemical Company also obtained U. S. patent 2,749,360 on esters of α - 2,4,5 - trichlorophenoxypropionic acids.

These new esters are said to be stable to light and air, non-corrosive to the skin of man and higher animals and of low volatility. They are suggested for use as plant growth regulators for purposes such as the prevention of sprouting of potatoes in storage, the induction of rooting of cuttings, and the prevention of premature abscission of pome fruits.

The following example taken from the patent illustrates the preparation of butoxypropoxypropyl ester α-2,4,5-trichlorophenoxypropionic acid:



$O(C_3H_6O)_2{-}CH_2CH_2CH_2CH_3$

47.57 grams (0.25 mole) of butoxypropoxypropanol, 74.12 grams (0.275 mole) of α-2, 4, 5-trichlorophenoxypropionic acid, 150 milliliters of ethylene dichloride and 1 milliliter of concentrated sulfuric acid were mixed together and heated at a temperature of about 95° C. for seven hours. Ethylene dichloride and water of reaction distilled out of the reaction zone and were condensed and separated, the ethylene dichloride being returned to the reaction vessel. Upon completion of the reaction, the product was filtered and washed twice with 100 milliliter portions of aqueous 10 per cent sodium carbonate solution and once with 100 milliliters of water. The washed product was then heated at a temperature of about 90° C. under a pressure of 20 to 25 millimeters and a current of air drawn through the product for a period of 3.25 hours to recover the ethylene dichloride solvent and remove traces of water. The undistilled residue was filtered to obtain the butoxypropoxypropyl ester of α-2, 4, 5-trichlorophenoxypropionic acid as a light yellow oil having an index of refraction (n/D) of 1.4987 at 25° C., a specific gravity (25°/25°) of 1.1910, a chlorine content by analysis of 24.3 per cent by weight and a saponification number of 126. The theoretical chlorine content and saponification number for the butoxypropoxypropyl ester of α-2, 4, 5-trichlorophenoxypropionic acid are 24.1 and 127, respectively.

Dextran Cosmetic Compositions

In recent years dextran showed its versatility by finding use as a blood plasma extender. Such use may become very important in the event of mass air attacks and one can only fervently hope that the effectiveness of dextran and other products intended for such use will never be put to the "acid test."

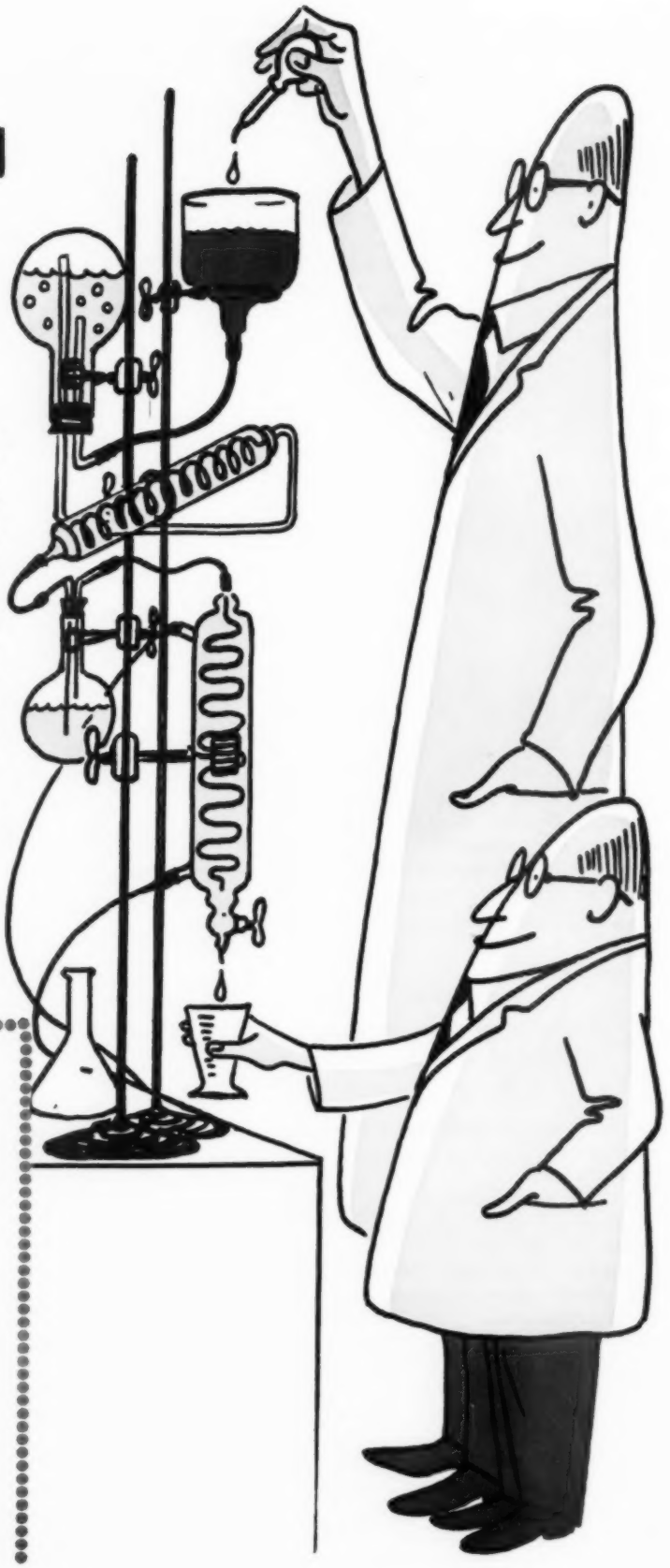
We now find that dextran is being suggested for use in connection with lipstick and skin-tinting cosmetic preparations, U. S. patents 2,749,276 and 2,749,277, having been issued recently in connection with these uses. The patents are assigned to The Commonwealth Engineering Company of Ohio, a patent holding organization.

U. S. patent 2,749,276 deals with the use of esters of dextran with fatty acids containing from eight to 18 carbon atoms as a base for lipsticks. It is claimed that the resulting lipsticks are water-repellent, firmly adherent to the lips, non-irritating, non-drying, non-cracking, non-smearing and non-staining. The patent states:

"The dextrans are high molecular weight, branched polysaccharides containing anhydroglucopyranosidic units linked together by molecular structural repeating linkages some of which are alpha-1, 6 linkages, others are non-alpha-1, 6 linkages and at least 50 per cent of these linkages being, apparently, alpha-1, 6 linkages. The dextrans vary with respect to their molecular structural repeating alpha-1, 6 to non-alpha-1, 6 linkages ratios, the extent of branching (the distribution and length of side groups or chains) their molecular weight, and their

(*Continued on page 116*)

SPECIALIZATION ...that's our business!



When it comes to the production of white oils, petrolatums and petroleum sulfonates, we think that our more than fifty years of background with these products justifiably earns us the title of *specialist* . . . a specialist who can be of genuine help to you whenever problems arise concerning the use of these highly refined products.

While our regular line includes many different types and grades of white oils, petrolatums and sulfonates, we specialize in tailor-making these products to fit specific needs. No matter what your problem may be, if it relates to a white oil, a petrolatum or a sulfonate—chances are we can supply a product that's exactly right for you . . . and that will give your product *special* advantages.

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NEWS...

Dedicate Rutgers-Colgate Lab

The Division of Dental Medicine of the Colgate-Palmolive Company in cooperation with Rutgers University was dedicated June 20. Ceremonies at the university were attended by some of the Nation's leading dental and industrial scientists.

For the first time, scientists especially trained in this field will staff an industry-supported laboratory exclusively devoted to basic studies in oral health. This partnership of Colgate-Palmolive research and the scientific facilities of Rutgers University is dedicated to expanding scientific knowledge of the oral cavity.

The new division will be primarily concerned with the biological sciences such as pathology, histology, pharmacology, histochemistry and bacteriology. Its scientists will explore such basic problems in dental medicine as the origin of periodontal disease, the causes of dental decay and the role of nutrition in dental health.

According to Dr. Thomas H. Vaughn, vice-president responsible for the Colgate-Palmolive Company's extensive research and development program, the company has long felt the logic of an active partnership of this type. Dr. Vaughn pointed out that in these academic surroundings the division's scientific work could flourish without interruption from immediate competitive pressures.

William Lee Sims II, president of Colgate-Palmolive, said, "The company thinks it singularly fitting that in this, our 150th Anniversary year, a Division of Dental Medicine should be established. It is our hope that from the research to be conducted in these laboratories will come new knowledge that may inspire other scientists to a better understanding of some yet unknown truths and prove of value to other industries, other researchers, and to all those working to benefit civilization throughout the world."

Dr. Lewis Webster Jones, president of Rutgers University, said, "Increasingly, industry has recognized an innate concern with research on the part of our institutions of higher learning. Their tendency toward partnership with universities in research is of great value to both."

The dedication was preceded by a colloquium at the Institute of Microbiology. Papers covering various aspects of dental health were presented by members of the division's staff.

Dum De Dum Dum

A Detroit policeman for eleven years before joining Parke, Davis & Company in 1949, Walter J. Bala has been named chief of plant protection for the company, according to an announcement.

Joins Hance Bros. & White

William H. Helfand has been appointed plant manager of Hance Bros. & White Co., Philadelphia.

At dedication ceremonies for the Division of Dental Medicine of the Colgate-Palmolive Company in cooperation with Rutgers University are, left to right, William Lee Sims II, president of Colgate-Palmolive Company; Dr. Lewis Webster Jones, president of Rutgers University; and Dr. Thomas H. Vaughn, vice-president of Colgate-Palmolive.

JOHN W. SOLOMON

Coty's Production V.P.

John W. Solomon has been elected vice-president in charge of production of Coty, Inc., Philip Cortney, president, has announced. With Coty since 1945, Mr. Solomon, for the past six years, has been plant and production manager.

DR. MARVIN SPIELMAN

Four Promoted by Abbott

Dr. Marvin Spielman's promotion from head of the organic research department to director of research evaluation is one of four promotions in the Abbott Laboratories research division announced by Elmer B. Vliet, vice-president and scientific administrator of the company.

Dr. Kenneth Hamlin has been appointed head of the organic research department to succeed Dr. Spielman. Dr. Richard U. Schock has been named assistant head of the department and Dr. Harold Zaugg has been promoted to the newly established position of research scientist.

Libraries Assn. Officer

Alberta Brown, head librarian of the Upjohn Company, was elected first vice-president and president-elect of the Special Libraries Association at the recent annual business meeting.

DOW

DOW PROPYLENE GLYCOL, U. S. P.

OUTSTANDING SOLVENT FOR HIGH-QUALITY SHAMPOOS

. . . excellent as a stabilizer and mutual solvent in many drug and cosmetic products

Their choice is Dow propylene glycol. We're talking about formulators of high-quality shampoos—with famous product reputations at stake.

These formulators have to satisfy their customers with the effectiveness of their product and with its dependability and absolute safety. Dow propylene glycol is the best possible solvent for such results—in shampoos and many other drug and cosmetic products.

Dependable in supply as well as quality, Dow propylene glycol will be shipped promptly from strategically located terminals. Your worries stop when you sign the order! You can obtain a sample and property information by writing THE DOW CHEMICAL COMPANY, Midland, Michigan, Dept. OR 854G-1.

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DOW

A pause for a pose at the American Society of Perfumers' dinner-dance held recently at the Hotel Pierre in New York.

Bristol-Myers Vice-Pres.

Orlin E. Johnson has been elected vice-president in charge of production of the Bristol-Myers Products Division. He was formerly assistant vice-president.

Joining Bristol-Myers in 1946 as an assistant department head, he has subsequently been in charge of the finishing department and has held the positions of assistant to the production manager and plant superintendent.

ORLIN E. JOHNSON

Gilbert Succeeds Bretschger

Frederick A. Gilbert has been elected president of the Becco Chemical Division of Food Machinery and Chemical Corporation, succeeding Dr. Max E. Bretschger who retired May 1, the 30th anniversary of his association with the company.

Stokes Changes Name

F. J. Stokes Machine Company, Philadelphia, has changed its name to F. J. Stokes Corporation. Stockholders approved the change at the company's recent annual meeting, Francis Dougherty, Stokes president, has announced. The new name was selected as being more in keeping with the broad range of the company's interests and the varied line of production and processing equipment which it has developed during the past 60 years.

Founded in 1895 by the late Francis J. Stokes as a manufacturer of hand-operated pharmaceutical tabletting presses, the company later developed power-operated presses, from which evolved today's fully automatic tabletting presses with outputs up to 4,000 per minute.

Often asked to assist in devising methods and equipment for preparation of pharmaceutical materials for tabletting, the company developed a line of dryers, mixers, drug mills and granulators, and revolving pans for coating and polishing tablets. Blood plasma was first prepared commercially on Stokes freeze-drying equipment by processes developed by Stokes scientists. Similar processes are used for the preparation of penicillin, streptomycin and other antibiotics.

Established to serve the needs of the pharmaceutical industry, Stokes today serves the majority of industries.

Eaton Veterinary Sales Mgr.

Warren L. Martin has been named manager of the new veterinary sales division of Eaton Laboratories, L. E. Daily, M.D., vice president, has announced. Mr. Martin has been a medical representative for the Wm. S. Merrell Co. and a veterinary representative for Winthrop Laboratories, Inc. He has also served as regional and East Coast and Canadian supervisor for Fromm Laboratories.

WARREN L. MARTIN

In New Lehn & Fink Post

Robert W. Naething, former Eastern regional sales manager for Lehn & Fink Division, has been promoted to the new position of special assistant for field operations at the New York office, according to an announcement by O. Glen Kennedy, division general manager.

Vitamins in Pharmaceuticals

A REPORT

Use of Biotin in Multivitamin Formulae

Biotin, now firmly established as an important member of the vitamin B complex, belongs in multivitamin formulae and dietary supplements for the reasons given below.

D-biotin is required for the growth of many organisms: animals, plants, bacteria. It appears to be related to the process of cell development. Symptoms of deficiency have been shown to occur in human beings who live on diets high in raw egg white.

Deficiency symptoms appear as severe dermatitis lesions, similar to seborrheic dermatitis and a desquamating disease of infants called Leiner's disease. These symptoms, when due to a deficiency of biotin, disappear after its administration. In animals, dermatitis, loss of hair, cessation of growth of the young and sudden death of the adults may occur.

Nearly 200 papers directly related to biotin research are in the literature. The work of investigation continues.

The evidence now available points to the need for biotin in multivitamin and dietary supplements which, by their very nature, are prescribed for therapeutic and prophylactic effect.

The Place of Biotin in Antibiotic Therapy

Rat feeding experiments using some of the sulfonamides show that the animals develop biotin deficiency. The same result has been found and reported from the use of antibiotics. It has been assumed that the same development might occur in man when this therapy is used. Under the circumstances, biotin should be included in stress formulae and in multivitamin supplements which are prescribed so often during and after the administration of these modern drugs.

Usage in Veterinary Medicine

In dogs and dairy calves it has been found that a deficiency of biotin will cause a paralysis of the hind quarters. This condition was cured by the administration of the vitamin. In chicks and turkey poults a biotin deficiency, represented by a dermatitis of the feet, may be overcome by the use of biotin in the feeding formula. A substantial increase in hatchability was found when hens were fed a ration known to be rich in d-biotin.

This evidence indicates that biotin has a definite place in veterinary medicine and animal nutrition.

Technical Data

Empirical Formula ..... $C_{10}H_{16}O_3N_2S$

Molecular Weight 244.3

Slightly soluble in water and 95% alcohol. Insoluble in ether, acetone and ethyl acetate. Soluble in d-panthenol.

Thermostable in dry crystalline form.

Not sensitive to light.

Not affected by reducing agents that may be present in polyvitamin and other pharmaceutical preparations.

The brilliant Roche synthesis of 1946 makes biotin readily available in pure form at a relatively modest cost.

Roche, a world leader in vitamin research and production, has a wealth of information about biotin. Skilled technical people are ready to help you incorporate biotin 'Roche' in your preparations.

New Edition of Brochure

Send now for your personal copy of the Roche technical brochure about d-biotin. Second edition is now available, complete with survey of recent literature and up-to-date bibliography. Ask your Roche salesman or write the Vitamin Division, without obligation.

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N.J. Control Group Elects

The Pharmaceutical Quality Control Group of New Jersey has elected the following to serve for the year ending March, 1957: Herbert I. Mitchell, chairman; Raymond L. Thatcher, chairman-elect; and Joseph W. Kouten, secretary and treasurer.

The group, whose function is to foster a free exchange of ideas on administration of quality control, consists of 30 members, representing 27 pharmaceutical firms in New Jersey and adjacent areas.

Pfizer Assigns Five

Five personnel changes in the chemical sales division of Chas. Pfizer & Co., Inc. have been announced. Willard K. Thayer has been named field sales manager of the division's Eastern region, and Robert C. Denman has been appointed manager of the division's industrial department.

Formerly sales representative in Southern California, John R. Post has been assigned to the headquarters staff of the medicinal chemical department in Brooklyn. Robert W. Johnson will serve the Oakland, Calif. area and Northern California, Southern Idaho, Utah and Western Colorado. Robert J. McGrath will serve Lost Angeles and the Southern California area.

Heyden's Western Sales Mgr.

Knox Price has been appointed Western regional sales manager of Heyden Chemical Corporation, T. M. O'Neil, vice-president in charge of marketing, has announced. Mr. Price will also continue as West Coast representative of Nuodex Products Company, a division of Heyden. Earl Hanson has been appointed Western regional representative to assist Mr. Price on both Heyden and Nodex activities.

Greeting Miss Lee Ann Merriwether, Miss America of 1955, at the annual CIBS ladies day luncheon are, left to right, Al Mosheim, House of Tre Jur, program chairman; George Kaempkes, Pacquin, first vice-president; David J. Warner, Fleuroma, president; and William Jaeger, Park & Tilford, second vice-president. Miss Merriwether, now with the NBC Dave Garroway television show, Today, was guest speaker on the program.

Merrell South Central Div.

A new South Central sales division, with headquarters in Memphis and covering a seven-state area, has been established by the Wm. S. Merrell Company. In announcing this, Frank T. Jacobs, vice-president in charge of marketing, named John Shipley as manager of the new division. For the past two years Mr. Shipley has been assistant to the sales manager of the Southeast division.

Carpenter on Shulton Board

Election of Frank N. Carpenter Jr. as a director of Shulton, Inc. has been announced by George L. Schultz, president. Except for service with the U.S. Army during World War II, Mr. Carpenter has been with Shulton since 1939. Elected a vice-president in 1952, he had previously held the positions of assistant to the president, sales manager and general sales manager.

Open Schering Canadian Bldg.

Dedication and opening of a modern plant and administration building in Montreal marked the 30th anniversary of Schering Corporation's operations in Canada. To symbolize the present and future growth of Canada and Schering Corporation, Ltd. a maple tree was planted by executives of the parent company, Francis C. Brown, president; Mortimer J. Fox, treasurer; W. H. Conzen, international division manager; and the vice-president of the Canadian subsidiary, Francis J. Gleason.

Architecture of the one-story building is functional, with red-brick facing dividing large window areas that line three walls of the office section. Future planning of both parent and Canadian companies stresses continued research and development of newer and more effective drugs.

Golden Working Anniversary

William Feger and James McKnight, who are celebrating their fiftieth year with George Lueders & Co., were honored recently in New York's Hotel Astor at a dinner-dance attended by all personnel of the company, including branch managers from San Francisco, Chicago and Montreal and salesmen from various parts of the country.

F. J. Lueders, president, presented diamond studded pins and wrist watches to the semicentenarians, who are the tenth and eleventh members of the Lueders Fifty Year Club. Three other members of the club are still active with the company: F. Weber, H. W. Heister, and August Miller.

KNOX PRICE

FRANK N. CARPENTER JR.

Memo to: **bulk users of**

AMMONIUM SULFATE
Purified, Granular

3 excellent reasons to buy Baker

❶ exceptionally pure
❷ controlled particle size
❸ fast-dissolving

SPECIFICATIONS

Assay $(NH_4)_2SO_4$	99.5	% Min.
Insoluble Matter	0.010	% Max.
Residue after Ignition	0.010	% Max.
Arsenic (as)	0.00003	% Max.
Heavy Metals (as Pb)	0.001	% Max.
Iron (Fe)	0.001	% Max.
Neutrality	Passes Test*	
pH of 5% Solution at 25°C	5.0-6.0	
Particle Size (Mesh)	At least 98% thru U.S. No. 20 Sieve	
	At least 90% thru U.S. No. 35 Sieve	
	At least 75% on U.S. No. 200 Sieve	

*A.C.S. neutrality test for reagent ammonium sulfate.

If Ammonium Sulfate is essential to your process, these three reasons can mean time and money to you.

Baker Ammonium Sulfate, Purified, Granular, is a product of synthesis.

It is produced from pure ammonia and sulfuric acid. This, plus Baker's precise process controls, yields an ammonium sulfate free of the usual impurities of by-product material. Its uniform granular particle size is fine enough to dissolve fast and provide trouble-free processing.

These valuable properties help minimize your processing and product variation, help decrease your production time, help *cut* your costs by the elimination of costly purification steps.

USES: Baker Ammonium Sulfate, Purified, Granular, finds particular application in industries requiring a material exceptionally low in critical impurities such as arsenic, heavy metals and iron.

Pharmaceutical —antibiotic manufa ture; preparation of biological seru precipitant in purifying and separati proteins; in blood fractionation.

Food Processing—in dry yeast produ tion and in leavening agents.

Fermentation—as an activating age nutrient, and for pH control.

Cosmetics—in formulations for hom permanent hair waving, in shampoos.

PACKAGING: Baker Ammonium Su fate, Purified, Granular, is packaged i fibre drums with net weights of 25, 10 and 300 pounds, and in bags of 10 pounds net weight.

The ability to produce fine and industri chemicals *of outstanding purity for proc ess and ingredient use* has made Bake a leading supplier for half a century.

Remember... it pays to buy Baker!

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Baker CHEMICAL

Baker Chemicals
REAGENT • FINE • INDUSTRIAL

CARL H. GERBERDING

Strong, Cobb Vice-Pres.

Dr. William E. Gaunt has been elected vice-president and director of laboratories of Strong, Cobb and Company, Inc., according to an announcement by John N. Eustis, president. During nine years with E. R. Squibb & Sons, Dr. Gaunt directed, in turn, product development, biochemical research and quality control.

Aromatic Is Newport Agent

Aromatic Products, Inc. has been designated by Newport Industries, New York, as exclusive selling agents for Menthol dl U.S.P. (Racemic) and Thymol N.F., according to an announcement by Newport.

The products will be sold throughout the country by salesmen of Aromatic Products working out of New York, Chicago, Dallas, Memphis, Pittsburgh, Los Angeles, Boston and Fort Lauderdale.

Ninol in New Plant

Ninol Laboratories, Inc., Chicago manufacturer of synthetic detergents and emulsifiers, has announced transfer of its research and development laboratories to a new plant at the south side of the city. Business and executive offices are being moved to larger quarters, the new address being: Ninol Laboratories, Prudential Plaza, Chicago 1.

New Post for Herslow

James F. Herslow has been appointed general sales manager of two associated firms: Sillscocks-Miller Company, manufacturer of plastic specialties, and Lusteroid Container Company, manufacturer of plastic vials and tubes, both of Maplewood, N. J. Mr. Herslow was formerly sales manager of Sillcocks-Miller.

Dragoco Forms U.S. Div.

The West German firm of Dragoco, Inc., producer of aromatic chemicals, perfume specialties and food and beverage flavors, has established a U.S. division, with offices at 432 Fourth Ave., New York.

The announcement was made by Dr. Henry G. Gribou, vice-president and general manager of the American division, a wholly owned subsidiary of Gerberding & Co., Holzminden, and its auxiliary Heinrich Haensel plants of Pirma. Dr. Gribou was formerly with Lever Bros. and Colgate-Palmolive.

Green Retires from National

Frank W. Green, associated with National Aniline & Chemical Division, Allied Chemical & Dye Corporation, for 37 years and in charge of the company's line of certified colors since 1927, retired last month. He has been succeeded by Arthur T. Schramm, associated with the company since 1936, and engaged in certified color sales at the New York general office since December 1953.

Mr. Green will continue to serve the company and its many customers for certified colors in a consulting capacity, according to H. J. Daigneault, vice-president.

Schering Promotes

James R. Hind has been promoted to office manager in the domestic sales division of Schering Corporation, Herman W. Leitzow, vice-president, has announced. With Schering since 1950, Mr. Hind was formerly branch manager of the company's West Coast office in San Leandro, Calif.

R. Blayne McCurry, president of Schenley Laboratories, Inc. and Mrs. McCurry at New York International Airport on their return from Europe, where Mr. McCurry, accompanied by George R. Gilbert, Schenley Laboratories vice-president in charge of international operations, spent four weeks in France, Spain, West Germany and Denmark meeting with officials of firms licensed to manufacture or package and sell products under the SchenLabs trademark.

DR. HENRY G. GRIBOU

Syntex, S.A. Board Elected

Election of a new board of directors for Syntex, S.A., Mexican steroid manufacturer, has been announced by M. L. Sindeband, executive vice-president of Ogden Corporation, which recently bought Syntex.

Newly elected directors are Milton Reynolds, Mexico City industrialist; Marvin Carton of Allen & Co., New York investment bankers; George Larrea, Mexico City business man; Malcolm Little of the Mexico City law firm of Goodrich, Dalton, Little & Riquelme. Directors elected to continue in office are Dr. George Rosenkranz, Licio Lagos, and Dr. Alexander Zaffaroni.

Dr. Rosenkranz was elected chairman of the board and managing director; Dr. Zaffaroni, executive vice-president; Mr. Reynolds, treasurer; and Mr. Little, secretary. Mr. Lagos will continue as president.

New Product Dev. Mgr.

Charles L. Lightfoot Jr. has been appointed manager of new product development for Monsanto Chemical Company's research and engineering division, St. Louis, it has been announced. Formerly assistant manager of government contacts in the development department, he will be transferred to Dayton, where the division's chemical research facilities are located.

Appointed by Borden

James R. Bodine has been named to the newly created post of director of sales and marketing for the prescription products division of The Borden Company, according to Dr. J. F. Muller, division general manager. Mr. Bodine will have complete responsibility for sales and marketing of the division's line of infant feeding and milk replacement products.

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Luis de Hoyas Jr., left, vice-president of Synfleur Scientific Laboratories, Inc., discusses "El Maguey," a painting by the noted Mexican artist, Jose Clemente Orozco, with members of Colgate University's Fine Arts Department. The painting is one of twenty-four from Mr. de Hoyas' extensive Latin-American collection which were recently exhibited at the university during Pan American Week.

MCA Elections Held

The Manufacturing Chemists' Association at its 84th annual meeting, held recently at White Sulphur Springs, W. Va., elected John L. Gillis, vice-president of Monsanto Chemical Company, as chairman of the board of the association, succeeding John R. Hoover, president of B. F. Goodrich Chemical Company. General John E. Hull, USA (ret.), full-time president and a director of the association, was re-elected.

Kenneth C. Towe, president of American Cyanamid Company, was elected chairman of the executive committee. Leland I. Doan, president of The Dow Chemical Company, and R. C. McCurdy, president of Shell Chemical Corporation, were elected vice-presidents of the association. M. F. Crass Jr., full-time secretary-treasurer, was re-elected.

Lauria Resigns

The resignation of Michael A. Lauria, vice-president and director of manufacturing for Strong, Cobb and Company, Inc., has been announced by John N. Eustis, president.

Nestle Buys Wisp-Stick

The Nestle Co. has bought inventory and trademarks of Wisp-Stick from Good Grooming Products of Detroit.

Form New Pharm. Firm

Capitol Laboratories, Inc. has been organized in Boston to manufacture and market medical specialties, including a group of silicone preparations, the first of which is Baby-Cote, a protective lotion for the prevention of diaper rash, bed sores and contact irritations.

Vick Names Sofskin Manager

Albert J. Elias has been appointed product manager of Sofskin Hand Preparations, it has been announced by Kirby Peake, president, Vick Products Division. Mr. Elias was formerly vice-president in charge of merchandising for Alfred D. McKelby Company, a Vick subsidiary, recently merged with another Vick subsidiary, Prince Matchabelli, Inc.

Whitney in New CSC Post

L. L. Whitney has been appointed superintendent of microbiological production operations for Commercial Solvents Corporation, with headquarters at the company's Terre Haute, Ind., plant. He will have responsibility for production of vitamin feed supplement and antibiotics.

With Commercial Solvents since 1947, Mr. Whitney has held the positions of superintendent of laboratories and process superintendent at the company's Peoria, Ill., plant.

LEONARD L. WHITNEY

Eastman Sales Dev. Section

Eastman Chemical Products, Inc. has created a new chemical sales development section, separate from its commercial sales department, according to an announcement by Dr. J. E. Magoffin, sales manager for the chemical division. The company plans to continue emphasizing the service nature of the laboratories in dealing with customer problems connected with the sale of products already on the market.

William M. Gearhart, formerly chief chemist in charge of Eastman's service and development laboratories at Kingsport, Tenn., has been appointed manager of the new section. R. B. Herring, who had served as assistant to Mr. Gearhart, has been promoted to chief chemist in charge of the laboratories, which will continue under Mr. Gearhart's supervision.

Under the new arrangement, all work with products being considered for the first time, and those in the development stage, will be assigned to the new section. Mr. Gearhart and his staff will have the responsibility for coordinating all laboratory work and industry contacts in bringing new developments to commercial status. At this point, responsibility for handling such products and establishing normal customer contact will be transferred to the commercial sales department and its field representatives.

New Private Label Co.

Pharmco, Inc. has been organized to serve the private formula trade in the drug and cosmetic industry and the chemical specialties field. Headed by Clarence Neuvirth, formerly chief developmental chemist at Strong, Cobb & Co., the newly formed company will provide research and development facilities for manufacturers and distributors of industrial and consumer products.

CLARENCE NEUVIRTH

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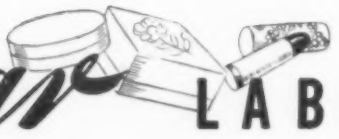

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Tufts Hon. D.S. to Tishler

Dr. Max Tishler, vice-president and executive director of Merck Sharp & Dohme Research Laboratories, received the honorary degree of Doctor of Science at Tufts University's centennial commencement June 10. The degree was conferred by Nils Y. Wessell, president of the university.

Dr. Tishler received his B.S. degree in 1928 from Tufts and later his Ph.D. in chemistry from Harvard University. Associated with Merck since 1937, he was appointed last March to his present post. He is a member of the National Academy of Sciences, the National Research Defense Committee, and many scientific societies.

Dr. Scheele to Warner-Chilcott

Dr. Leonard A. Scheele has resigned as Surgeon General of the U. S. Public Health Service to become president of Warner-Chilcott Laboratories Division of Warner-Lambert Pharmaceutical Company. Dr. Scheele, forty-eight years old, has spent all his professional life (twenty-three years) in the Health Service. He became Surgeon General in 1948, and began his third term last April 16.

Join Polak's Frutal Works

George Charles Coquel has joined the perfume laboratories of Polak's Frutal Works, Inc. and William H. Kanninen, the flavor laboratories, according to an announcement by the company.

Toni Buys Charm-Kurl

Charm-Kurl recently was purchased by The Toni Company, according to R.N.W. Harris, Toni president.

GENE D. WILKEN

B-M Sales Promotion Dir.

Gene D. Wilken, formerly division sales manager of Bristol-Myers Products Division on the West Coast, has been appointed director of sales promotion for the company, with headquarters in New York, according to an announcement by E. Lloyd Bernegger, executive vice-president. Prior to joining Bristol-Myers, Mr. Wilken was vice-president in charge of sales of Johnson & Johnson's Tek-Hughes division.

Boyer Receives Hon. LL.D.

Francis Boyer, president of Smith, Kline and French Laboratories, received an honorary Doctorate of Laws at the 109th annual commencement of the Hahnemann Medical College, Philadelphia.

Appointed by Robertet

Donald Heithaus has been appointed Mid - Western representative for P. Robertet, Inc. and Tacanic Natural Oils. He was formerly with Procter & Gamble.

THOMAS R. CALLERY

Callery Joins Bristol Labs

Thomas R. Callery has been appointed director of the special products division of Bristol Laboratories, Inc., Richard A. Anderson, vice-president and director of marketing has announced. Mr. Callery will make his headquarters at the company's New York office. He was formerly manager of the pharmaceutical chemicals division of Commercial Solvents Corporation.

Vick Product Managers

Jack N. Highsmith has been promoted to product manager for cough drops for Vick Products Division, and John S. Scott has been promoted to product manager for cough syrup.

van Ameringen-Haebler Dir.

Election of Chester F. Smith to the board of directors of van Ameringen-Haebler, Inc. has been announced by Charles P. Walker, president. Formerly president of Esso Standard Oil Company, Mr. Smith is a director of Standard Oil Company (New Jersey), where he has served as vice-president and a member of the executive committee.

Vice-president of the American Petroleum Institute's Refining Division in 1949 and 1950, Mr. Smith has been decorated by the French Government as a Knight of the Legion of Honor and by the Belgian Government with the Order of Leopold.

Rhodia's Mexico, Cuba Reps

Rhodia, Inc. has appointed Comerciale Reka S.A. as sales and technical representative for synthetic aromatic chemicals and compounds and "Alamask" industrial reodorants in Mexico, with offices in Mexico City, and Luis Felipe, Havana, as representative for these products in Cuba, according to an announcement by Rhodia.

A double-header birthday celebration, sponsored by Magnus, Mabee & Reynard, Inc., was held at India House, New York, recently to mark the 60th birthday of Joseph Baird Magnus, left, and the 55th birthday of Robert B. Magnus, right, vice-presidents of the firm. Joining in a three-way handshake is Percy C. Magnus, president of MM&R.

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Drug Firms Form Guild

A group of manufacturers and packers in the drug and related fields has formed a new trade association known as The Drug and Allied Products Guild. Purposes of the Guild are to "endeavor to improve general economic conditions and foster better relations between themselves, the retail trade, the wholesale trade, and their suppliers."

Officers of the Guild are: president, Leonard Brown, Mifflin Chemical Company, Philadelphia; first vice-president, Claude S. Welton, Purepac Corporation, New York; second vice-president, Martin Schugar, Pennex Products Company, Pittsburgh; third vice-president, Julius Richter, Twin City Manufacturing Company, Norfolk, Va.; treasurer, J. F. McCambridge, McCambridge & McCambridge Company, Riverdale, Md.; secretary, Edward Roseman, Adde Company, Baltimore; executive secretary, Eugene S. Stringer, Philadelphia; chairman of the executive committee, David C. Gross, Integrity Magnesia Corporation, Philadelphia.

Directors of the Guild are: Jack Starr, Standard Drug Company, Newark, N. J.; I. Goldstein, Cumberland Manufacturing Company, Nashville, Tenn.; Jack Kaplan, Diamond Drug & Magnesia Company, Revere, Mass.; Herman M. Shapiro, Myron Drug, Baltimore, Md.; James B. Wright, Davis Manufacturing Company, Knoxville, Tenn.

Robert J. Brecker, of Kleinbard, Bell & Brecker, has been retained as counsel.

Felton's Baude in U. S.

Jean-Paul Baude, with the Montreal and Versailles plants of Felton Chemical Company, Inc. for the past seven years, has joined the company's expanding American perfume staff. A veteran of twenty-five years in the perfume industry, he was formerly with Lautier Fils and Mero Boyveau of Grasse.

JEAN-PAUL BAUDE

Chem. Buyers Elect Spencer

S. E. Spencer, purchasing agent for the Wm. S. Merrell Company and recently appointed coordinator of purchases for Vick Chemical enterprise companies, has been elected national chairman of the Chemical Buyers' Group of the National Association of Purchasing Agents, according to an announcement. Other officers elected were:

J. W. McKinney of E. I. du Pont de Nemours & Co., first general vice-chairman of the group; Robert G. Weigel, Eli Lilly & Company, second general vice-chairman; Carl De Prima, Hoffmann-La Roche, Inc., chairman of the pharmaceuticals and fine chemical section; Robert Wier III, Hercules Powder Company, chairman of the heavy and industrial chemical section; D. W. Massengill, S. E. Massengill Company, secretary; and J. W. McNeil, Pittsburgh Coke & Chemical, treasurer.

C. W. TARBET

Armour Labs Sales Dir.

C. W. Tarbet has been appointed sales director of The Armour Laboratories, E. L. Patch, general manager, has announced. J. C. Libby has been appointed personnel manager.

Asst. to Eaton Med. Editor

Abraham Mittelmark has been appointed assistant to the medical editor of Eaton Laboratories, L. E. Daily, M.D., executive vice-president, has announced. Boris Anzlowar is medical editor.

Hon. LL.D. to Gilmore

Donald S. Gilmore, the chairman of the board and managing director of The Upjohn Company, received an honorary Doctor of Laws degree at the recent commencement exercises of Kalamazoo College.

CARL PACIFICO

Pacifico Is Vice-President

Carl Pacifico has been appointed a vice-president of American Alcolac Corporation, according to an announcement. He will continue to manage the development department but will also assume additional responsibilities in directing the company's sales program.

Matchabelli-Seaforth Moves

Offices of Prince Matchabelli Inc. and the Seaforth (A. D. McKelvy) Company have moved to 415 Madison Avenue, New York 17. Simonetta Inc., a subsidiary of Prince Matchabelli, is located at the same address.

William H. Gesell

William H. Gesell, 65, former vice-president in charge of manufacturing for Lehn & Fink Products Corporation, died June 6 in Montclair, N. J.

Paul H. Hyde

Paul H. Hyde, 67, former president of the Mentholatum Company, Buffalo, died June 22 while playing in a golf tournament at the Highland Golf and Country Club, Indianapolis, during a heavy rain.

A golfer since boyhood, he won the Kansas State amateur championship in 1908, was captain of the Williams College golf team and Buffalo district champion six times. He was one of six sons of the founder of the Mentholatum Company, the late Albert A. Hyde.

Surviving are his wife; his son, Edward K. Hyde II, who is vice-president of Mentholatum; two daughters; three brothers; and two sisters.

Edward Nalin

Edward Nalin, president of Nysco Laboratories, Inc., Long Island City, N. Y., died May 13.

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Management Forum

by Francis Chilson
INDUSTRIAL CONSULTANT

Idea Creation

The other day I learned of an organization which specializes in stimulating creative thinking and they organize—at a price—executive groups to show them how it is done. Essentially the idea is this: a group of men get together with a pre-arranged topic for discussion. Everybody present lets his mind run wild and suggests all sorts of ideas as to how a product, process or procedure might be improved. No thought of cost or practicability is allowed to interfere with the flow of suggestions. When everybody has exhausted his imaginative capacity, the suggested ideas are winnowed out. The wildest ones are discarded and the remaining list is re-examined to select the most workable ideas. These are again re-examined to see if any of the ideas can be combined. The residual idea or ideas is then developed. The process is called "Brain storming." One of its proponents was on Dave Garroway's show. (One must have a word and if one gets the right word he can sell it.)

This process has been one of my favorite techniques for at least twenty-five years. I never thought there was anything new or remarkable about it. Twenty years ago at Norwich for example we followed this technique regularly—generally in some comfortable bar or hotel room where there would be no interruptions. In making ointments for example, we concentrated on the mixing process as it is carried out everywhere from concrete mixing to dough mixing. The result was that we came up with a combination mixer and mill originally used for dispersing pigments in lacquer—the Abbe Lenart mixer. When we introduced it for making Unguentine we reduced the processing time per batch from thirty hours—which it had been formerly—to less than three and the product was better.

We did the same thing in connection with inserting cotton into tablet bottles. The net result of our cogitations was a plunger to insert the cotton rope, equipped with fingers like an expansion bolt that would shove the cotton under both shoulders simultaneously. Lakso happened to drop in one day and we gave him our ideas, which Lakso then reworked into the first automatic cottoning machine used in the industry.

At that time Norwich was the third largest producer of milk of magnesia in the U. S. It was made by the double decomposition process, which required a hell of a lot of water and a hell of a lot of space for the settlers. So by the bull session method described above we came up with the idea, that since magnesium sulfate is itself an electrolyte, all we needed was an electrolytic cell. We made one and it worked up to a point. The thing that stopped us was that the cathodes became coated with the amorphous magnesium hydroxide magma and insulated them to such an extent that electrolysis stopped. We put the problem up to the cell makers and they displayed little interest in working out a way of removing the magma film as fast as it formed. Norwich then became interested in magnesium hydroxide paste produced from sea water. This was so cheap and simple to handle that further work on electrolysis was dropped. I am convinced that had we gone on with it we could have developed a continuous discharge cell.

At Burroughs Wellcome during the war, when we were confronted with the problem of producing 20 million onion skin ampouls of iodine and a similar quantity of amyl nitrite—a quantity of ampouls never heard of in the trade up to that time—we had a bull session similar to the ones I conducted at Norwich. I was impressed with the extraordinary number of novel ideas that were suggested—some very good ones from men who had had neither technical training nor production experience. The resulting concentration of ideas resulted in a conveyorized setup, which took the ampoules straight through filling, sealing, tubing, tube sealing, boxing and packing for final shipment.

If you want some gray hair try sealing an onion skin ampoule filled with anything containing a volatile solvent such as tincture of iodine or amyl nitrite. But it was done and done on a mass production basis never heard of before or since.

I could recite hundreds of similar cases running all through my experience. The idea of the bull session of "Brainstorming" if you prefer is a good one. It must be kept informal and everybody must be encouraged to speak up regardless of how ridiculous or wild a suggestion may seem. A wild idea can trigger somebody else's mind as readily as a tame one. I have found that a lot of men are afraid to speak up especially in the presence of their bosses or their mates because they are afraid of being ridiculed then or later. They must be encouraged to let their hair down and I have found that a slug of whiskey or two helps to remove inhibitions.

ADMA—APMA Merger?

An official announcement of the first meeting of the joint legislative committee of the two drug associations mentioned above, indicates the possibility of a merger of the two. The idea is being given serious study. Such a merger is bound to come. It is ridiculous for any industry to maintain two associations with a common purpose and identical memberships.

But I think, as I said in this column a year or two ago, that the Proprietary Association should be included too. Some members of the proprietary Association are also members of the other two associations and a good many of the ethical firms are owned by proprietary firms.

I think it is high time to get rid of the notion that there is any real difference between ethical firms and proprietary firms except in the manner of advertising. Doctors tell their patients to buy Bayer Aspirin or Phillips Milk of Magnesia in spite of the fact that these products are advertised to the public. On the other hand every ethical firm in the country would be in a hell of a fix if it lost its proprietary business, *i.e.*, the stuff that is sold over the counter without prescriptions. I can name some ethical firms whose over-the-counter business is three times their prescribed business.

Squibb has sailed along all these years, advertising their proprietary items to the public, yet enjoying an exceptional reputation among the doctors for their ethical items.

If it were proposed to define ethical drugs as those which are dangerous, habit forming or impossible to administer without professional aid, and if it were proposed further to restrict ethical firms to the manufacture of these drugs only, there'd be a hell of an uproar. So why don't we cut out the nonsense and recognize that all drug manufacturers have identical problems in all phases of their business and all stand together, not only for their own but the public welfare. In unity there is strength.

I work in both divisions of the drug business and I find the people in the proprietary division to be just as honorable as their ethical colleagues. I doubt if there is a single, established firm in the proprietary side of the business that would try to sell a dangerous drug regardless of how big the potential market was. I have found that quality control is just as thorough in the proprietary end of the business as it is anywhere else. The Norwich Pharmacal Co., which is a proprietary firm although it is a member of both ethical associations, has made a fetish of exhaustive quality control for many years, and, without question has done as much as any firm in any branch of the industry to put quality control on the high plane it is today.

The mechanics of a consolidated association would have to be worked out. The consolidation of all drug manufacturers into one association would present a problem in getting space enough in one hotel to hold national meetings. But the ADMA has already pointed the way in separating scientific, and production engineering sections from the annual meeting, which is primarily administrative. A consolidated association could have separate meetings for separate sections: administration, legal and finance; production and engineering; research; marketing and advertising; quality control.

Sales Training Aids Co.

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Water

Water is getting to be a precious as well as a necessary commodity in this industry. Reports are made from all over the country of falling water tables and wells that were formerly good producers going dry. I'd like to call the attention of the larger manufacturers to the Ranney-Method Water Supplies Inc. system of producing water in large volumes even in areas where water supplies are low. Unless you are using at least a quarter of a million gallons of water daily this system is too expensive for you. The Ranney method consists of sinking a cassion into the ground a distance of fifty or seventy-five feet. From

this cassion horizontal bores are driven in every direction like the spokes of a wheel. These bores or horizontal wells are fitted with perforated pipes to pick up ground water seepage which flows back into the cassion, which thus serves as a water reservoir as well as a pump house. The Ranney Method is remarkably effective and the system is in use all over the world. DuPont has several installations—one producing over a million gallons a day the year around. Lilly has one, too, in their Lafayette plant.

The Outfit is located in Columbus, Ohio. Incidentally if you are planning to build a new plant, don't buy the land for it unless the purchase contract contains a clause that permits you to drill for water at your own expense to make sure it is there. When used in large quantities water is a costly commodity if you have to buy it from city sources, and it is getting so that some cities are putting a limit on the amount they will sell you.

London Consultant

When I was in London recently I had a damned good dinner in a joint in Soho with my friend, Fred Wells, editor of Soap Perfumery and Cosmetics. As a result of his training in chemistry and his experience in perfumery Freddie can sniff a bottle of wine and tell instantly whether the girl who tramped out the grapes had washed her feet. If she hadn't the wine is better. Something to do with bunions. I've met many a tramp in all walks of society but I've never met a grape tramp. She must have lovely purple legs. I suppose if they slip and fall they get purple bottoms too. I wouldn't know. You'll have to ask Freddie. He's an authority on purple language and purple bottoms.

Apart from his editorial responsibilities Fred is an authority on and operates a separate consulting business in perfumery and cosmetic chemistry. In my book Fred's O.K. So if you should need a European consultant Fred's your man. 9 Gough Sq., Fleet St., London, E.C. 4.

Nepotism

The following quotation from a recent issue of Time shows how wide-spread is the foul practice of nepotism. There is plenty of it in both the drug and the cosmetic industries. A company president who condones nepotism not only should be fired; he should be put in jail. A president is a trustee for all stockholders not just a few.

"Featherbedding occurs at top level management and extends down to the rank of foremen," said A.I.M. in a report to its 17,000 members. And one of the biggest causes of featherbedding is nepotism. In more than half of the 23,000 U.S. companies A.I.M. studied, an executive had put his sons, cousins, brothers—even an assortment of relatives—on the payroll.

In every field of U.S. industry, A.I.M. found other examples of executive featherbedding. It cited the case of the two Eastern banks that merged and ended up with four vice presidents who had nothing to do, and the case of the New England manufacturer who booted his incompetent production manager upstairs to "vice president in charge of personnel," where subordinates handled the job he was supposed to do. Many a corporate head creates positions to make work for friends, said A.I.M., and some invent titles merely to surround themselves with yesmen. Asks A.I.M.: "How can management, in all fairness, complain at labor featherbedding when managements are so widely guilty of the same practice? In management featherbedding, the damage is greater, the cost is larger and the bad example is more obvious."

Let me tell you the story of how Ed Austin once exercised his trusteeship.

I have always had tremendous admiration and respect for Ed Austin, president of Leeming and Pacquin. But my respect increased enormously when Ed summarily fired his nephew because that young man, having been put into the factory to learn the business from the ground up, decided that, because his mother was a big stockholder in the company and his uncle president, he could and would do what he damned well pleased. The young man was not amenable to discipline and was causing serious trouble in the plant. When Ed learned about the situation he promptly took action regardless of his personal feelings and regardless of the possibility that it might precipitate a family row.

It was a fair and honorable action and the only one he should have taken in the circumstances. It was indeed the only action Ed would have taken, being the fair minded man he is. And in the long run it was good for the boy too. But "blood is thicker than water" and there are very few men in industry big enough to have done what Ed did. It is needless to say that Ed not only cleared the atmosphere but he snapped up sagging morale and earned the undying loyalty and respect of his entire organization. I wish that all company presidents were as honorable and as faithful to the trusteeship vested in them as corporation presidents as Ed Austin proved himself to be.

England Wising Up

Alarmed at her scientific position, and in spite of the attitude taken by Cambridge as discussed here recently, England has announced an emergency $271,000,000.00 five year plan for scientific and engineering education. Her position in engineering—all branches—may be indicated by the fact that at the present she is educating 57 engineers per million of population while the U.S. is graduating 136 and Russia 280.

Brandt & O'Dell

When I was in London recently I had the pleasure of meeting Paul Brandt, senior partner of the firm

How to save up to 6¢ per unit

on your AEROSOL PRODUCT

It doesn't take a very sharp pencil to figure the profit you are losing when you ship your aerosol product from an eastern or mid-western warehouse to the west coast. Depending on the method of shipment, it can easily add 2¢ to 6¢ per unit to the cost!

No longer is it necessary to sustain these losses. By taking advantage of G. Barr & Company's new Los Angeles aerosol filling plant, high transportation costs can be EXTRA PROFITS for you and your west coast customers need not wait days for merchandise to arrive from the east . . . it can be made in the same market as it is sold.

With three complete, strategically located plants available—New York, Chicago, Los Angeles—arranging your custom aerosol production can be simplicity itself. Only one management to deal with, yet all three plants operating in accordance with the same high standards to exactly meet your specifications.

Whether your aerosol product is packaged in metal or glass, in thousands or millions of units . . . whether you have a product now on the market, or in the experimental or idea stage, you cannot afford to overlook the production and product development facilities G. Barr & Company provides.

We will be pleased to present exact figures.

WRITE, WIRE OR PHONE:

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named in the heading. This is an engineering and architectural firm which operates throughout the British Commonwealth. One of the most impressive laurels of the firm is that they have been retained by the U. S. government, not only for projects abroad, mostly military installations, but also in this country as well. What impressed me most however was the amount of industrial work this firm has done. I met the chiefs of the heating and ventilating, electrical and mechanical divisions and it didn't take long to discover that they really know their stuff.

Brandt & O'Dell, on industrial work, operate what they call a "turn key job;" that is to say they will locate the plant site, do all the engineering and architectural work, build the plant, install the machinery and turn over to you an operating plant. In other words they are comparable to Austin in this country. (I neglected to mention before that they have a staff of 130 architects and engineers of all kinds.) An important point for American firms contemplating the erection of a plant anywhere in the Commonwealth is that Brandt & O'Dell will arrange financing if necessary.

A point in which Hoffmann-La Roche, Geigy, Sandoz and Ciba will be interested is that Paul Brandt, although a British subject, was born and trained in Switzerland. This won't account for his wide experience but it may help to account for his thoroughness. The address of the firm is 12 Queen Anne St., London, W1.

It is a great pity I did not have the good fortune to meet Paul Brandt before getting involved with a supercillious British architect, who knows nothing about industrial construction and had never worked on an industrial plant before, although he represented himself to my clients as an experienced industrial architect. As it turned out after he had been hired he had designed only a relatively small industrial research laboratory. I managed to knock out, after a series of battles, all his cock-eyed ideas as they affected the factory and many of the more costly and useless construction features of his architectural design. Yet in spite of all this, the building will cost when finished as much per square foot as a similar building would cost in this country, where labor costs are three times as high as they are in England. That's the penalty one must pay for the services of an inexperienced industrial architect. The factory will be well and expensively built—far too much so for an industrial unit.

As a matter of fact there are very few good independent industrial architects in England. Judging British architects by the appearance of the factories one sees in England, one would say there are *no* good independent factory architects in England. The average English factory one sees in driving through the country side looks bloody awful. When you do see a plant that looks neat and attractive you can bet your bottom dollar it is an American plant, although many American plants over there, designed by British architects, are bloody awful too. How approval was secured for such monstrous abortions I wouldn't know. The artistic conceptions of British architects, as reflected in factory design, still reflects the taste of that ugly German goose, Queen Victoria. It is odd that this should be so because British small house architecture is cozy and generally good—undoubtedly because the architects haven't tried to innovate and are still copying the designs of the Tudor and Georgian periods.

So if you're contemplating a plant in England get hold of Brandt & O'Dell. Their architects have had experience working with Americans and, even if they are not as imaginative as American architects, you will get a soundly conceived and engineered, and an economically built factory too. And that's what counts in factory construction.

Again Conformity

"*You must adjust* . . . This is the legend imprinted in every schoolbook, the invisible message on every blackboard. Our schools have become vast factories for the manufacture of robots. We no longer send our young to them primarily to be taught and given the tools of thought, no longer primarily to be informed and acquire knowledge; but to be "socialized" —which in the current semantic means to be regimented and made to conform. The modern report card reflects with horrible precision the preoccupations of our teachers and the philosophy of our educators. Today in the public schools grades are given for the 'ability' of a child to 'adjust' to group activities, for whether he is 'liked' by others. . . .

"Must we conform?" The answer is a resoanding No! No . . . not only because in the end we are creatures who cannot conform and who are destined to triumph over the forces of conformity; but No because there is an alternate way of life available to us here and now. It is the way of positive rebellion, the path of creative protest, the road of productive revolt. This is the way natural to man, the way he must and will take to achieve the values he aspires to just because he is human. By taking it man can find the future of which he dreams, the future in which he will achieve his far, high, and unforeseeable goals . . ."
—*From "Must You Conform." by Robert Lindner (Rinehart).*

AMEN!

New Johns-Manville Mineral Filler

Want to absorb liquids or control viscosity? Try *Micro-Cel*—it absorbs up to six times its weight in water, remains a free-flowing powder even after absorbing twice its weight in liquids.

Want to bulk up your compound for better control

(Continued on page 98)

for making press-coated tablets

The new Stokes press-coating machine produces press-coated or dry-coated tablets to a high level of uniformity and precision. These machines make tablet-within-a-tablet structure commercially practical. This technique opens up broad possibilities for unique products.

. . . for applying coatings where water cannot be used

. . . for combining incompatible materials

. . . for producing heavy or time-delay coatings at low cost

. . . for making multiple-dosage tablets

The machines produce tablets consisting of a core surrounded by an accurately controlled layer of compressed dry material. Core tablets, prepared on a standard press, are automatically hopper fed to the press coater. The machine first fills the die volumetrically with a portion of the coating granulation. Then a core tablet is centered in the die cavity, and the remaining coating material is filled in, and pressed accurately to required density.

These operating features assure dependable, uniform production:

- Core tablets accurately centered
- Easy set-up and changeover of core size or coating
- Coating thickness accurately controlled on all sides
- Automatic rejection of core-less tablets
- Embossing or engraving of coated tablets
- Uses standard tooling

Write for complete specifications, and for a consultation on your specific application.

Put your new product ideas with these *new* Stokes Tablet

for making multi-layer tablets

New Stokes multi-layer rotary tablet machines now make it possible to manufacture tablets which have several layers of different ingredients . . . to precise weight tolerances in each layer. This technique proves useful for such products as multi-color tablets . . . preparations with two active materials separated by an inert layer . . . simultaneous dosages of incompatible materials . . . and numerous other specialized tablets.

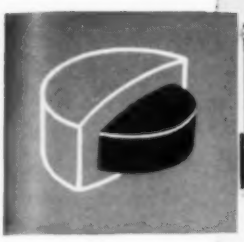
In the new Stokes machines, each layer is pressed separately. Weight tolerances of 1% or better are readily maintained. Each layer is separated cleanly from the others.

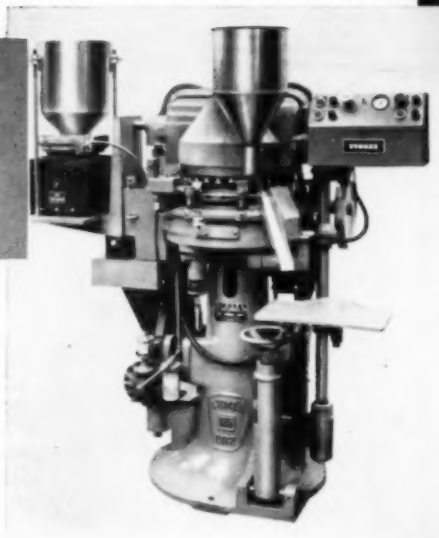
A single set of cams can produce a variety of multi-layer tablets. A three-layer press can be changed over easily to produce two-layer or standard tablets. While the machine is in operation, the first and second layers can be ejected for weight check.

Several different models are available, all using standard BB-2 punches and dies. Production is conservatively rated at values up to 950 tablets per minute.

FIND OUT TODAY how these new Stokes tablet machines can help you put new ideas on the market . . . at economical cost. Contact your nearest Stokes office, or write for complete facts . . . on these machines, and on the Stokes Advisory Service.

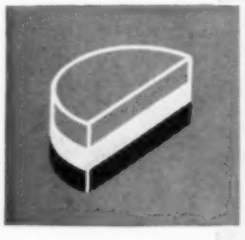
F. J. STOKES CORPORATION, ***Pharmaceutical Division,*** **5510 Tabor Road,**

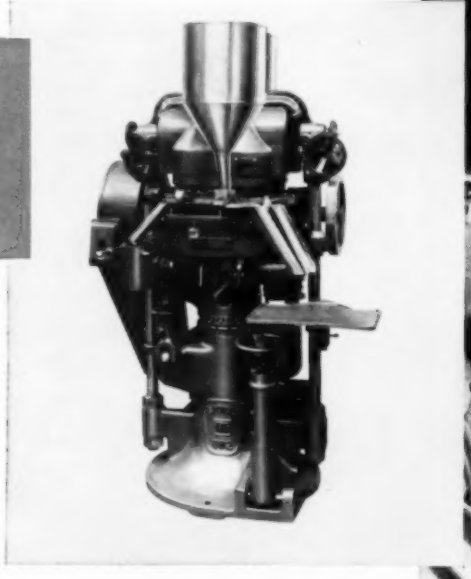




Core tablets are fed into the hopper, then automatically fed to the transfer mechanism, and coated accurately to desired thickness and densities.

to work Machines





Individual layer compression assures close weight tolerances per layer. Here the operator is ejecting first layers of multi-layer tablets for weight check, while the machine is in operation.

Phila. 20, Pa.

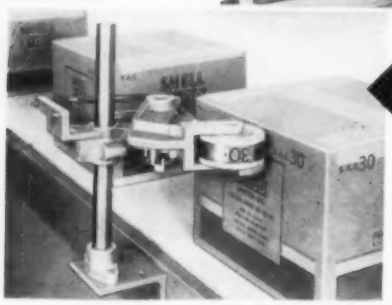
STOKES

Coding Problem?

Check with Gottscho

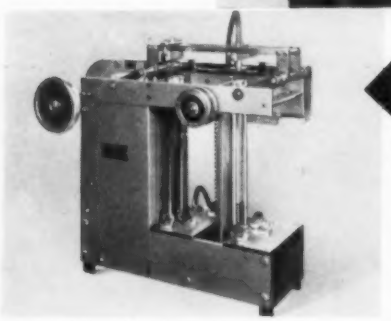
. . . automatic code-dating machines for every package, every purpose

Top-Coder . . . imprints code-dates, other changeable legends on top surface of round or rectangular cans, canisters, jar covers, cartons, boxes. Attaches to conveyor or packaging machine. Locates imprints accurately even if container flow is irregular or intermittent.



Side-Coder . . . imprints side surfaces of folding cartons, set-up boxes, rectangular cans and canisters. Can be used to imprint codes, product identification, etc. simultaneously. Fully automatic, adapts to any mechanized production-line.

Bottom-Coder . . . portable, space-saving unit that imprints codes on bottom of jars, bottles, cans, etc. Imprint surface may be flat or concave, flush or recessed. Wheels right up to the line, can be moved about at will.



Label-Coder . . . foolproof, automatic bench unit that imprints codes on labels in bulk. Imprints up to 5 different legends on labels in a single run. Handles full hour's capacity of labels without attention . . . delivers them in perfect stack.

Write for descriptive bulletin, specifying machine in which you are interested

Gottscho **ADOLPH GOTTSCHO, INC.**

Dept. C, Hillside 5, N. J.

Automatic Production-Line CODING, MARKING, IMPRINTING MACHINES
In Canada: RICHARDSON AGENCIES, LTD., Toronto & Montreal

(Continued from page 95)

of package density? Try *Micro-Cel*—a cubic foot weighs as little as five pounds.

Want to prevent caking? Try *Micro-Cel*—its high absorption works wonders in controlling deliquescent products.

Want to extend pigments or reduce surface sheen? Try *Micro-Cel*—it combines fine particle size, large surface area and inertness with high absorption suggesting many applications.

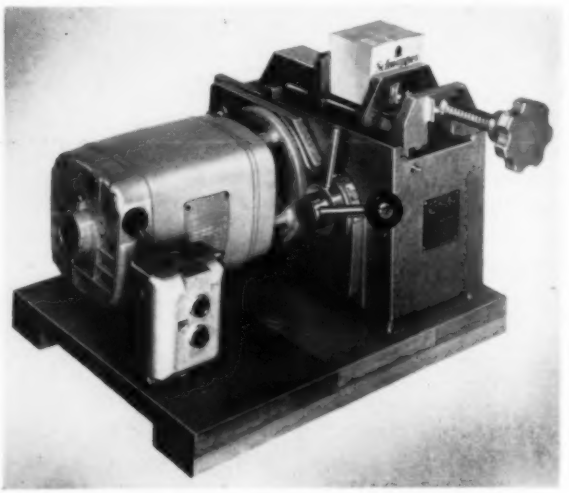
Want to assure better suspension of heavy solids? Try *Micro-Cel*—its particle size, as low as .02 micron, provides uniform dispersion and blending.

Micro-Cell is a brand-new line of synthetic calcium silicates produced by combining lime with diatomaceous silica under carefully controlled conditions.

The inert properties of this new product suggests its use a possible replacement for all or part of the starch used in tablet making. The fact that it will absorb six times its weight of water suggests the possibility that the agglomerates thus formed might exercise the same mechanical action in disintegrating a tablet that starch does. This might be particularly true if this material is used in combination with a wetting agent. I haven't had a chance to experiment with this product in making tablets but it seems worth a try. In any case its physical properties suggest many applications in the manufacture of pharmaceutical and cosmetic products. You can get samples by writing Johns-Manville, Box 60, New York 16. Be sure always to mention this magazine as the source of your inquiry.

Label Dating Machine

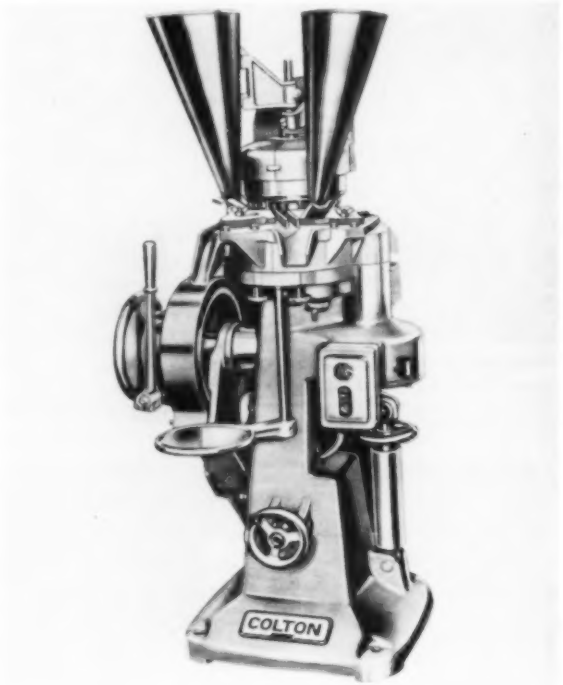
Labels of all sizes and shapes, including round and oval, may be coded in packets of up to 500 or more at



a time with Codedge, Mark 11, distributed by Griffin-Rutgers Inc., 41 East 42nd Street, New York 17. The machine has an output of 2,000 labels per minute.

Two- and Three-Layer Tablet Presses

Two new models of rotary tablet presses for producing two- and three-layer tablets have been added to the line of single-rotary tablet presses made by

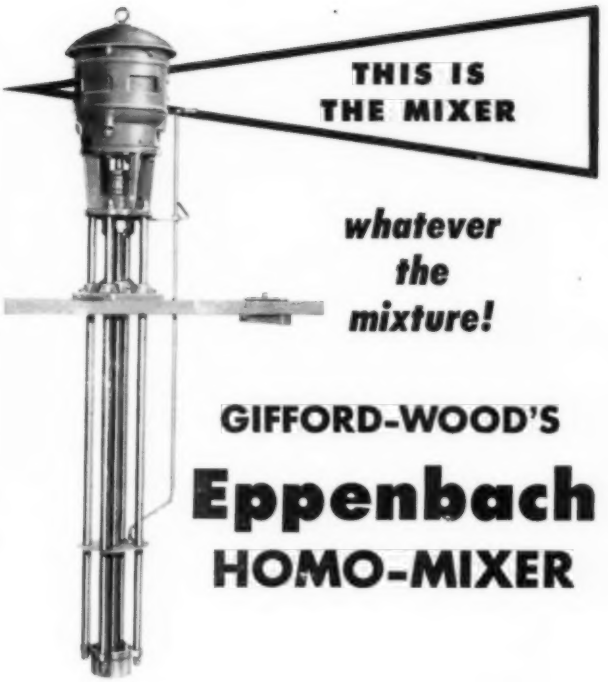


Arthur Colton Company, 3109 East Lafayette, Detroit 7. Designated as the Model 212 (above) for producing two-layer tablets, and the Model 213 for three-layer tablets, these presses are designed to provide manufacturers with machines having exceptionally low tooling costs and production rates up to 1,000 tablets per minute.

The Model 212 will produce 1,000 two-layer tablets per minute with diameters up to 5/8 in. and total fill up to ¾ in. The Model 213 will produce 800 tablets per minute with diameters up to 5/8 in. and 9/16 in. total fill. Both models have 16 punches and dies.

Both models can produce a single-layer tablet without changeover. They can be converted to a single hopper standard model with a parts kit. They have three-point mounted feed frames, fiber scrapers at leading and trailing edges of the feed frames, special right and left hand aluminum guards with dust removal chutes and a discharge chute. The 212 two-layer model can have a first layer up to 11/32 in. fill within the ¾ in. total fill limit. The 213 three-layer model permits a 7/16 in. total first and second fill within the 9/16 total fill limit, with a possible ¼ first fill. Punches and dies are the same as used in the standard 216 Model.

Each press provides a maximum tablet pressure of 6,000-pounds and is powered by a 1½ hp motor. They occupy a floor space about 28 by 30 in. and are 61 in. high.



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A high speed, high shear homogenizer-mixer for complete, "no-vortex" mixing of chemicals, cosmetics and pharmaceuticals to produce emulsions of small particle size and long shelf life.

Check these features:

- Continuously draws material from the bottom of the tank, thus eliminating a vortex and minimizing air intake.
- Easily adjustable deflector plate to control flow pattern.
- Stationary or portable operation.
- Homogenizing head dismantles easily for cleaning.
- All immersed parts of stainless steel.
- Can be modified to suit existing processing requirements.
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- Laboratory and production sizes.

FREE Eppenbach Catalog No. 402R-2 describing HOMO-MIXER Models and accessories. Write for it. Also ask about the famous Eppenbach Colloid Mills and Agi Mixers and G-W Chemical Feeders and Breakers.

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MERCHANTS' MAN IN CINCINNATI calls the manufacturer, locates several drums of the chemical at the plant of a nearby soap company. They agree to lend three drums to meet the emergency. Merchants' truck makes the pickup.

AT MERCHANTS' WAREHOUSE, the drums are loaded into the car of "Dutch" Spatta, manager of Merchants' Cincinnati office. Regular delivery by truck will take too long.

A FAST 108 MILES LATER "Dutch" delivers the drums in time to keep production going. It was somebody else's product and somebody else's problem, but Merchants again lived up to its reputation for helping a customer out of a jam.

WHY MERCHANTS' CINCINNATI MANAGER DROVE 108 MILES TO DELIVER SOMEBODY ELSE'S PRODUCT —

At Merchants, service goes beyond the mere filling of orders for industrial chemicals. Each office of Merchants' nationwide chain makes a point of becoming familiar with its customers' problems. In the past 35 years Merchants has frequently "walked the extra mile" to help a production man out of a tight spot. Among the products offered are acids, alkalis, fungicides, surfactants, chlorinated solvents, emulsifiers, laundry compounds, soaps, dry ice and chemical specialties.

MERCHANTS CHEMICAL COMPANY, INC.

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Compounder's Corner

Baby Oil Aerosol

F. J. A. Bateman in the British Medical Journal for March 10, 1956 reported on the use of a silicone barrier cream for the treatment and prevention of bedsores and results were very good. Since then, the Journal has carried correspondence on the use of this product for preventing and treating diaper rash, again with laudatory comments.

We would like to suggest that for both these protective applications, as well as others, but especially in the treatment and prevention of diaper rash, an aerosol package seems ideally suited. In this form, a thin layer of protective oil, silicone alone or mixed with other water-repellant ingredients would be sprayed where needed in a thin layer and could then be gently rubbed into the skin if desired. As a matter of fact, the protective material could be formulated as an aqueous liquid emulsion and then combined with the propellant mixture, but this would seem to be an unnecessary duplication, both the emulsifying process and the aerosol valve being intended to furnish active ingredient in the form of finely divided droplets.

As concerns the use of aerosols containing oils on and around infants, the user should be cautioned to apply the preparation in such a way as to avoid inhalation of the finely divided oil by the baby.

Zinc Oxide Hyperfine

Zinc Oxide Hyperfine according to J. B. Conn et al. (*S. Am. Pharm. Assoc. Sci. Ed.* 45:311, 1956) is produced by low-temperature calcination of zinc carbonate ammoniate. It possesses unusual physical properties: the color is brick red, the particle size is about 200 A, it is hygroscopic, and cements in water. Heating at temperatures exceeding 400° causes it to revert to ordinary zinc oxide. X-ray diffraction evidence indicates disorder in the crystal lattice together with extremely small particle size as being responsible for the observed effects.

The hygroscopicity and possibly also the cementation effect can be accounted for in the sorption of water in the porous structure left by abstraction of ammonia and carbon dioxide from the zinc carbonate ammoniate crystal. These physical characteristics likewise lead to enhanced chemical reactivity. Copeland and Brauer, for example, have shown that the setting of zinc oxide-eugenol dental cement is a consequence of reaction to form an eugenolate, and that this reaction is very much faster and more extensive when Zinc Oxide Hyperfine is used. It therefore offers advantages in topical formulations which employ zincoxide.

Polysol Aerosols

Connecticut Chemical Research Corp. has announced variation in aerosol manufacture that promises certain advantages. These are embodied in the use, alone or in combination with customary propellants, of certain "fixed" gases including helium, neon, argon, carbon dioxide and others. Along with these gases, new type valves and processing methods have been developed.

Advantages claimed for the Polysol concept include reduced corrosion, possibility for use internally and freedom from chilling. Investigation is continuing for the application of this procedure to the formulation of antiperspirants, mouth washes, inhalants and other personal hygiene items.

Depilatories

Depilatories based upon calcium thioglycolate, either made in situ from thioglycolic acid and calcium hydroxide or added as the finished salt to the cream base are not completely satisfactory. Although they are effective in removing hair, the time required is often as much as ten minutes, which may be excessively annoying. The slow action of the calcium thioglycolate is probably related to its low solubility and its easy conversion from an active internal salt with a molecular weight of 184 to a virtually inactive dibasic salt with a molecular weight of 222. For faster action, according to T. Ruemele (*Seifen-Ole-Felle-Wachse*, 82:273, 1956) either a more easily soluble thioglycolate, or some corresponding ingredient, must be added. Thus, increasing the pH of thioglycolate waving solution will give, with a cream base, a useful depilating composition.

Another important factor in the depilatory preparation is the cream base. The high alkalinity must be taken into consideration and only components resistant to hydrolysis should be considered. Because of alkalinity, and also because of discoloration, the composition of the tube is important.

Depilatories are not simple products, but require special study for effectiveness and uniform results and this can only be accomplished by technical study.

Kylan

Kylan is deacetylated chitin, obtained from shrimp shells by the Kylan Corporation of Spartanburg, S. C. The product is a polymer of glycose amine related to aminocellulose and is a fiber- and film-forming material. It is a cationic protective colloid and can be used as an emulsifying and stabilizing agent. Possible applications to cosmetics are obvious; present applications include the imparting of shrink-resistance to wool fabrics, improving the water resistance and bursting strength of paper, antistatic treatment of fibers, the preparation of oil-well drilling muds, etc.

Fluorescent Hair Brighteners

Detergent shampoos containing certain fluorescent brighteners have now been patented in France (pat. no. 1,094,336). The fluorescent compounds selected for this application belong to the group of substituted 4-methyl coumarins. They are substantive to hair in a solution which is weakly acidic. The compound 4 - methyl - 7 - diethyl-

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(HEXACHLOROPHENE U.S.P.)

with its unique degerming and antiseptic action, was the key to increased sales and broadened markets *for all these products:*

SOAPS

Waterless Hand Cleaners
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Deodorant
Antiseptic
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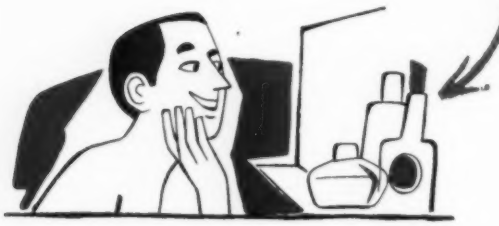

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Menthol Lotions and Ointments
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Skin Conditioners
Dusting Powders
Hair Dressings
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SINDAR® *Corporation*
Industrial Aromatics and Chemicals
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aminocoumarin is particularly effective for imparting highlights to hair. Another optical bleach recommended for use in shampoos is 4-methyl-5, 7-dihydroxycoumarin.

The fluorescent compounds are incorporated in shampoos which are based on sulfated detergents. The list of suitable detergents includes sulfated lauryl alcohol, the sulfated monoglyceride of coconut fatty acids and sulfated alkanolamides. These are used in the form of their ammonium or ethanolamine salts which are highly soluble in water. Although the fluorescent coumarin derivatives are only slightly soluble in water, they dissolve in concentrated solutions of the sulfated detergents. A small proportion of alcohol may be included in a clear shampoo to make sure that the optical bleach remains in solution when the shampoo is exposed to low temperatures.

The 4-methyl coumarins show the greatest substantivity to hair in shampoos having a pH value between 4.5 and 6.5. The acidity of the detergent solution may be adjusted by the addition of either a mineral acid or an organic acid. The foaming and cleansing properties of the sulfated detergents are not adversely affected by mild acidity.

4 - Methyl - 7 - diethylaminocoumarin has a definite brightening effect on hair when used in shampoos at a concentration of 0.2 per cent. However, higher concentrations up to a maximum of one per cent may be preferred.—*Schimmel Briefs.*

Suppository Bases

The problem of rectal absorption was discussed by Gradnick, who indicated that the rectal mucosa had a high absorbent capacity, comparable to that of the mucosa of the small intestine. Once absorbed, the greater part of the drug appears to be first taken up by the portal system, and only a small proportion, by by-passing the liver, enters immediately into the general circulation. Gradnick also pointed out the importance of the media used in the preparation of the suppositories, fatty media giving slow, prolonged absorption, whereas water - soluble media liberate their medicaments more easily and should be used when a rapid effect is required. Given a suitable base, it has been stated that absorption of quinine and the barbiturates rectally is as quick as when given by mouth. Emulsifying bases can be expected to be intermediate in effect but melting point and emulsifying power are also important. Gradnick has stated that substances which have a high activity in small doses are better administered *per rectum*. The kinds of medicaments usually administered *per rectum* fall into two main groups: Those required to act locally, e.g., anesthetics, astringents, protectives and antiseptics, and those with a systemic action, e.g., analgesics, antibiotics, hormones, aminophylline, mersalyl and chlorpromazine. Medicaments intended for local use should be incorporated in a fatty base, and those for systemic action in a water-soluble or emulsified base with a low melting point.

According to J. Soulsby and S. J. Hopkins (*Pharm. J.* p. 157, 1956) the official fatty base is cocoa butter, a substance which possesses many of the properties of an ideal base and which is well known to all pharmacists. Nevertheless, it has disadvantages which must be recognized. The most important, from the pharmaceutical point of view is that if it is heated to just above its melting point an unstable modification is formed which has a much softer consistency, a lower melting point, and a prolonged solidification time. These changes in the character of the base make the preparation of suppositories without the aid of an ice-box very difficult. The unstable modification reverts to the stable form after a few days' storage and becomes granular in appearance.

Many attempts have been made to find alternative bases. Bird suggested the use of propylene glycol monostearate, together with a small proportion of sodium or ethanolamine stearate. The liberation of incorporated medicaments from this base depends more on hydrophilic properties than a low melting point. Thus, insoluble substances would be kept in intimate contact with the tissues, whereas water-soluble drugs would diffuse out and be absorbed. Another approach to the problem was adopted by Caldwell who investigated the use of hydrogenated oils as suppository bases, and who recommended hydrogenated palm-kernel oil, particularly for tropical use.

A more recent and superior product is stated to consist of "glycerol esters mainly of lauric acid to which a very small amount of glycerol monostearic acid ester has been added to improve its water-absorbing capacity." It is white, odorless and non-irritant. Hard to the touch, it moulds very easily and contracts on solidification, so that it leaves the mold without the need of a lubricant and the surface of the suppositories has an attractive high gloss finish.

High molecular weight polyethylene glycols may be used as a suppository base. A wide range of these glycols is available, ranging from liquids to hard wax-like solids, so that by blending, products of any desired consistency and melting point can be obtained. The lower molecular weight members are miscible with water in all proportions, and the higher members are partially miscible, so that the incorporation of aqueous solutions is simple. These bases are solvents for many chemicals; they also dissolve lipophilic substances and are therefore suitable vehicles for oil-soluble drugs. Since suppositories prepared with these bases are soluble in water, a body-temperature melting point is not essential as they will eventually dissolve in the rectum. These glycol bases are well tolerated, and offer interesting alternatives to cocoa butter.

Boric Acid

A questionnaire of the opinion of dermatologists regarding the use of effects of boric acid sent out by R. S. Fisher (*A.M.A. Arch. Dermatol.* 73:336, 1956) was answered by more than 65 per cent of those certified by the American Board of Dermatology and Syphilology. Among those responding, 94 per cent used boric acid in their practice, 71 per cent indicating frequent usage. It is a widely held clinical impression that boric acid exerts a useful bacteriostatic effect in both wet preparations and the ointment.

Forty-eight physicians commented, "Boric acid is safe in ordinary usage." Twelve stated, "There is danger only in infants or when applied to large areas of denuded skin." Thirty-seven indicated they do not use boric acid on extensive eruptions or on infants. Twenty-one, including four professors of dermatology, volunteered that they consider the danger of boric acid poisoning overrated. Thirty said that boric acid could be replaced or they considered other agents better. Half of this 30 were in the group of nonusers of boric acid. Six commented specifically on the inexpensiveness of boric acid in this age of increasing cost of medical care. Several indicated they prefer boric acid for home use because its inherent limit of solubility at less than five per cent prevents the patient from doing himself harm by overenthusiastic strengthening of the solution. Finally, 56 wrote that they have used boric acid for many years without observing any toxic effects.

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Advancing Therapy

Calories

I am pleased to find scientific justification for my preference for driving a car over walking—the energy expenditure while walking is 6.6 calories per minute while driving requires only 2.8 calories. If you save energy when you can, it will be there theoretically when you need it, which is merely a not very convincing rationalization.

In any event, *The Sugar Molecule* for Spring 1956 reprints interesting and useful tables of energy expenditures for various recreations as reported by R. Passmore and J. V. G. A. Durnin in *Physiological Reviews* for October 1955. Dancing the foxtrot utilizes 5.7 calories per minute as against 7.0 calories for the rumba (no mention of jitterbugging); weeding the garden consumes 4.4 calories, but digging uses 8.6; golf calls for 5.0 calories, tennis 7.1, while swimming uses up to 11.5 calories per minute.

Aspirin Substitutes

4-Hydroxyisophthalic acid was identified as the main constituent of the brown dust residue left from the sublimation of crude salicylic acid, another by-product being the 2-hydroxyderivative. Preliminary pharmacological evaluation showed these compounds to be potent antipyretics and mild analgesics. Detailed pharmacology by H. O. J. Collier and G. B. Chesher (*Brit. J. Pharmacol.* 11:20, 1956) was done with rabbits and rats. The 4-derivative, intraperitoneally, showed antipyretic activity as great as that of aspirin and the 2-compound was also active. The 2-and the 4-compound were about equally active as analgesics, more potent than aspirin but less active than salicylamide and codeine. The 2-hydroxyisophthalic acid was less toxic than codeine, aspirin or salicylamide, while the 4-compound was even less toxic.

The analgesic activities of some related acids in comparison with 4-hydroxyisophthalic acid equal to 1.0 were phthalic acid 0.4, isophthalic acid 0.4, terephthalic acid 0.5, 3-hydroxyphthalic acid 0.3, 4, 5-dihydroxyisophthalic acid 0.9, hydroxyterephthalic acid 0.7, 2,3-dihydroxyterephthalic acid 0.6, trimesic acid 0.5, hydroxytrimesic acid 0.5, 2,4,6-trihydroxybenzoic acid 0.5.

Comment: Acetylation and esterification are only two of the possibilities for modifying the structure of these analgesic, antipyretic compounds that will occur to the medicinal chemist seeking to improve activity and reduce side reactions. Cost is, however, a most important factor in attempting to capture a substantial part of the aspirin market.

Leritine Analgesic

A new analgesic compound, Leritine (generic name anileridine) has been tested by Merck & Co. in animals and in human beings. It has been found to be about twice as active as meperidine and although less likely to cause addiction it is subject to narcotic regulations. The compound is the ethyl ester of 1-(4-aminophenethyl) - 4 - phenylisonipecotic acid, which differs from meperidine by the replacement of a methyl group by the aminophenethyl group. It was developed and evaluated by a group including J. Weijlard, P. D. Orahovats, A. P. Sullivan, Jr., G. Purdue, F. K. Heath and K. Pfister, 3rd.

Novobiocin

Novobiocin is the generic name for a new antibiotic isolated independently by Merck, Upjohn and Pfizer. The Merck trade name is Cathocin, of Upjohn is Albamycin and is Cardelmycin for the Pfizer product. Its properties were reported in a series of papers by an Upjohn group in *Antibiotics and Chemotherapy* 6:135, 1956.

Novobiocin is a new antibiotic, active against gram-positive and gram-negative microorganisms in vitro. It is produced by a streptomycete isolated from soil and identified as a new species, *Streptomyces niveus*, n. sp.

The antibiotic is a dibasic acid having the approximate formula $C_{30-32}H_{38-42}N_2O_{11-12}$. It is distinguished from known antibiotics by melting points, optical rotation, ultraviolet and infrared spectra, crystallographic properties, and potentiometric titration. Novobiocin is more soluble in basic than in acid solutions. The acid solutions, however, are more stable. Numerous salts have been prepared.

Novobiocin was active in vitro against many gram-positive bacteria and a few gram-negative organisms. In vitro end points against the coliform and enteric bacterial groups were variable and depended on the strain being tested. In mouse-protection studies, it was highly effective against *M. aureus*, *Past. multocida*, and *P. vulgaris* infections. Moderate in vivo activity was observed against *Str. hemolyticus* and *D. pneumoniae*. At the levels tested, it was inactive in *S. typhosa*, *S. paratyphi* B, and *Ps. aeruginosa* infections.

It was effective in a wide variety of media, and the optimal *p*H was near neutrality.

Novobiocin was administered to dogs, mice, and human volunteers in order to ascertain its pattern of absorption, distribution, and excretion.

Unusually high and well maintained serum levels were attained, with peak values occurring two to four hours after administration when the antibiotic was given orally to human subjects and dogs in amounts that were anticipated to be in the therapeutic dosage range. In mice, on the other hand, somewhat lower levels were attained, and the peak values occurred within an hour. A comparison of the serum concentrations attained using various routes of administration in dogs showed that the oral route gave peak values intermediate between the intravenous and intramuscular.

Novobiocin was distributed widely throughout the body tissues and fluid of dogs following oral administration. Somewhat higher concentrations were found in the liver and large intestine

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than in other tissues. The concentration in the bile was approximately 16 times that in the serum and urine.

Approximately one third of an orally administered dose was accounted for as biologically active material in the feces of dogs. Only about one-hundredth was present in the urine.

Antiviral Vaccine

The Army now has a successful vaccine against the virus pneumonias, grippe and other cold-like diseases that attack recruits in training.

The diseases are called ARD, short for acute respiratory diseases. They are caused by a virus, and are severe enough to send a man to the hospital. They are not the same as the common cold.

The number of such cases was cut by more than 80 per cent in trials at Fort Dix, N. J., the Army announced.

The new vaccine gives protection quickly, reaching maximum effectiveness within one week. Army medical officers are particularly enthusiastic about this because it means they can stop epidemics before they start sweeping through training camps.

The viruses against which the new vaccine protects cause more than half of all hospitalized cases of respiratory disease in military recruit camps. At Fort Dix about 20 per cent of all the men who train there during the winter are put into the hospital because of this illness.

The new vaccine was developed and prepared by the Army's department of respiratory diseases, headed by Dr. Maurice R. Hilleman, Walter Reed Army Institute of Research, Washington. It was evaluated in soldiers at Fort Dix by a field team headed by Maj. Reuel A. Stallones and Dr. Ross L. Gauld of the Institute.

It is made from tissue cultures of monkey kidney that had been infected with the two predominant RI viruses. These are also called ARD and APC viruses. The virus in the vaccine was killed with formaldehyde. The vaccine caused no untoward effects in the more than 350 persons who got it.

Although the new vaccine is still considered to be on a testing basis, more and more recruits will receive a protective shot.—*Science News Letter*, June 2, 1956.

Oral Antidiabetic Drugs

Two new oral antidiabetic arylsulfonylureas, N_1 - sulfanilyl - N_2 - n - butylcarbamide (BZ55) and N_1-p-tolylsulfonyl - N_2 - n - butylurea (U2043 or Orinase), are under intensive investigation according to A. R. Colwell (*Diabetes* 5:62, 1956). These substances in single oral doses will lower the blood sugar promptly and substantially in normal men, dogs, and rabbits; hypoglycemic effects occur within an hour or two (earlier when given with alkali) and persist for hours. Abnormal glycosuria and hyperglycemia can be reduced or eliminated by these compounds in many patients with mild or moderately severe diabetes mellitus; Franke and Fuchs reported eight cases where this happened, and they claim similar results were obtained in 80 per cent of 50 diabetics treated in Berlin for periods up to one year. Bertram, Bendfeldt, and Otto reported the successful control of diabetes following the use of a sulfonamide in 25 of 28 older patients with mild diabetes who were not using insulin and in 28 of 38 patients in which the compound was substituted for insulin. The sulfonamide had no effect in younger patients with severe forms of diabetes.

Toxic side effects seem to be negligible with the compounds, and the LD_{50} dosages in animals are high. Skin reactions may occur, but hematologic, hepatic, and renal effects are seldom noted.

Investigators agree that the compounds are totally ineffective in "pancreatectomy diabetes" and relatively ineffective in alloxan diabetes.

No compounds of this type are on the market at the present time and intensive investigations concerning indications, mechanism of action, and particularly dangers from continued use are being carried on by two pharmaceutical firms which are testing the compounds in diabetic patients in selected clinics and laboratories.

Carbutamide, a sulfonamide derivative, has been administered by A. S. Ridolfo and W. R. Kirtley (*J.A.M.A.* 160:1285, 1956) to 31 diabetic patients. Given by mouth, it was found to be absorbed rapidly and excreted slowly, so that satisfactory responses were achieved with maintenance doses of 1 gm. per day. Attempts were made to maintain a level of at least 10 mg. per 100 cc. of blood.

Reduction of hyperglycemia was accomplished with carbutamide alone in some cases. In other cases, the carbutamide reduced the insulin requirement. It was not satisfactory in young persons with unstable diabetes or in the emergency treatment of diabetics in acidosis. Side-effects that occurred in one case were temporary.

The effectiveness of orally administered carbutamide in lowering the blood sugar leval indicated that it should be useful in many cases of mild or moderately severe diabetes.

New Pharmaceuticals

Atarax (J. B. Roerig & Co.), an ataractic drug, is used to induce peace of mind quickly in the non-psychotic person under emotional stress. It is indicated in conditions such as tension, anxiety, hysterical reactions, climacteric, neurosis, fatigue states, etc. Therapeutic effect begins within 15 minutes, reaches maximum level within two hours after administration and generally lasts six to 20 hours. Atarax is said to be free from major side effects and toxicity. It is available in 10 mg. orange and 25 mg. green coated tablets in bottles of 100.

Flexin (McNeil Laboratories), generic name zoxazolamine, is an orally effective drug for the relief of muscle spasm in musculoskeletal and neurological disorders. It is available as 250 mg. scored yellow tablets in bottles of 50. The chemical compound is 2-amino-5-chlorbenzoxazole.

Aqua-B, Ascorbic Acid (Upjohn) is an injectible vitamin composition. Each cc. contains thiamine hydrochloride 12.5 mg., riboflavin 3 mg., pyridoxine hydrochloride 1.5 mg., d-pantothenyl alcohol 15 mg., nicotinamide 50 mg. and ascorbic acid 75 mg. It is available in 10 cc. vials for intravenous or intramuscular administration.

Demerol with Atropine (Winthrop) is supplied in 2 cc. ampuls for intramuscular or subcutaneous injection, each cc. containing 50 mg. Demerol hydrochloride and 1/300 grain atropine sulfate and is sold in packages containing 25 ampuls. **Demerol with Scopolamine** it available in 30 cc. vialt, each cc. containing 50 mg. Demerol and 1/300 grain of scopolamine hydrobromide. **Demerol with A.P.C.** is available in bottles of 100 tablets. Each tablet contains Demerol hydrochloride 30 mg., aspirin 200 mg., phenacetin 150 mg. and caffeine 30 mg.

Tri-Synar Plus (Armour Laboratories) is a sedative-antispasmodic combination containing in each lavender-colored tablet 4.1 mg. powdered extract of belladonna, 20 mg. of phenyltoloxamine, 12.5 mg. of ethaverine hydrochloride, 2.025 mg. of phenobarbital, 2.025 mg. of sodium butabarbital, 6.075 mg. of sodium pentobarbital and 6.075 mg. of sodium secobarbital. It is intended to provide parasympathetic sedation and generalized sedation and is available in bottles of 100 tablets.

(Continued from page 37)

effect on the foaming power of alkyl sulfates and aralkyl sulfonates, but the others are virtually unaffected. Soap apparently does not affect foaming power in the presence of soft water, but with hard water the foam is either completely destroyed or greatly reduced; finally, in the presence of a water softener like a phosphate or carbonate, the foaming agent and the soap seem to regain compatibility.

Powder bubble baths may contain from 10 to 75 per cent of surface active substance, the rest being filler (along with perfume and color). The filler must not be chosen, however, solely on the basis of low cost, since it can perform a useful function; as much as possible of the filler should be active water-softener compounds. These can include carbonates, polyphosphates and possibly the addition of sequestrants might prove useful. Synthetic gums are sometimes included to improve foam stability.

Liquid bubble bath preparations may contain from 10 to 50 per cent of the active ingredient, depending upon its solubility as well as cost. Where possible, a water softener should also be included.

There has been some writing about possible combination of effervescent mixtures with bubble baths so that bubble preparations would generate their own bubbles; this we believe to be largely a delusion. The volume of effervescent mixture required to generate sufficient gas for the bubbles would be absolutely prohibitive.

Another point that seems to intrigue manufacturers and consumers alike is the problem of making a bubble bath preparation that will provide bubbles not destroyed by soap. It is likely that the answer can be found in the combination of the right surface active agent and water softener. Maybe this stability to soap is not actually as desirable as is thought, however. In the mechanics of the operation, the preparation is poured into the stoppered tube and the water turned on full force until bubbles fill the tub. After a period of relaxation in the tub the bather gets down to the business part of the operation, applies sufficient soap, and the bubbles diminish or disappear. The water softening effect and the perfume still remain and the tub is quickly emptied and rinsed. If the original volume of bubbles remains, however, rinsing the tub can be a real chore and the overall use of the preparation be less attractive.

As has been repeatedly emphasized, there is no reason for bath salts to consist of inert sodium chloride crystals serving no purpose other than as a carrier for color and perfume. Water-softening is easily and cheaply accomplished by selection from a variety of compounds. The requirements for a bath salt compound include stability to temperature and atmosphere, suitable crystal size and shape, quick solubility, ease of handling in the tinting and perfuming operation, suitable cost and water-softening power. Choice is usually made from one of the forms of sodium carbonate: decahydrate, monohydrate or the compound with sodium bicarbonate known as the sesquicarbonate. The first forms large crystals which tend to effloresce in dry atmospheres (this can be controlled by use of a humectant such as glycerin in the coating operation) and will melt if the temperature is at all elevated. The monohydrate, which dissolves a little more slowly, is available in a variety of crystal sizes and is completely stable. The sesquicarbonate, as attractive small needles, is stable and very quickly soluble in the bath water. Borax, sometimes recommended, tends to dissolve slowly, trisodium phosphate is too alkaline, while the tetrasodium pyrophosphate is a mildly alkaline water softener. With due regard to crystal size and shape to avoid segration during mixing, mixtures of various water softeners with cheaper inert fillers can sometimes be made advantageously.

Little has been said about color and perfume up to now. Perfume especially will go a long way in determining whether or not the product sells well. Selection may start from the variety available for soap perfuming because, except in the case of bath oils, bath preparations tend to be alkaline and will destroy or alter a poorly chosen perfume. This is also the case with colors.

In solid mixtures, powders or crystals, the perfume and color, after proper proportions have been determined, can be mixed with alcohol or other suitable volatile solvent and added in portions to the batch in the mixer. Spraying, although it entails some loss of perfume, is sometimes advantageous in the case of small batches. Liquids as a rule cause few manufacturing problems; where the perfume or other oil does not have sufficient solubility in the carrier, alcohol or a glycol may be useful in forming a homogeneous mixture.

TABLET COATING . . . WET AND DRY

(Continued from page 39)

pear. Then 91 per cent isopropyl alcohol is likewise poured over the tablets until they lose their stickiness. Hot air is now blown on the tablets until they are thoroughly dry. By this method, large quantities can be handled at one time with but small quantities of solvents.

For a proper coating set-up, expensive equipment is needed.[12] Coating pans range in size from 12 inches to 48 inches in diameter and are constructed of galvanized iron, copper and stainless steel.[20] The last of these is least reactive to drugs although all three types may be coated with varnish before reactive tablets are subcoated. Canvas drums or additional pans are required for the polishing step. In order to evaporate the moisture from the successive coats, a forced air system capable of moving air at 120-150 c.f.m. with a maximum air temperature of 190° F. is employed.[17] This air is introduced into the pans through metal ducts containing dampers for the con-

(Continued on page 118)

Perfumer's Shelf

Oakmoss

Oakmoss is to be found in many parts of the world, but several countries have instituted high customs duties on oakmoss products as a protective measure. Oakmoss is found not only on the oaks themselves but also on many other trees, particularly on pines, firs, spruces and fruit trees. That from oaks (or genuine oakmoss) provides the best oils; they have a green color and a by-odor of iodine. These oils are the genuine "oakmoss oils." The oakmoss from conifers (pines, firs, etc.), or "treemoss," gives oils of an inferior quality, with a greyish-green color and a resinous by-odor.

The best oakmoss and treemoss is gathered during Summer. Natural oakmoss products employed in perfumery are tinctures, concrete and absolute oils, resinoids, liquids oils, decolorized and colorless oils, distilled oils.

Usually oakmoss is extracted with benzene to yield a highly colored concrete oil. This oil may be extracted with alcohol to obtain a colored absolute oil. The absolute oil is solid at room temperature and is therefore sometimes mixed with an odorless liquid solvent: either diethyl phthalate, ethyl citrate or castor oil, or a mixture of these three solvents. In order to obtain special qualities, soluble resinoids of orris, storax and myrrh, decolorized absolute oil of labdanum, cedar wood oil are added.

Because of their dark green color, the several absolute oils of oakmoss and treemoss must be decolorized when they are used in a high proportion in perfume. Usually concrete oils and resinoids of oakmoss are not decolorized. Only absolute oils can be decolorized easily. Absolute oils of Oakmoss are decolorized by activated carbon by fractionating at reduced pressure, by fractionation of the absolute oils with aid of glycerine, and distillation of the absolute oils in a current of steam.

Sesquiterpene Oxide

During his investigation of the constitution of sesquiterpene compounds, Treibs established the constitution of germacrol, alpha-kessyl alcohol and caryophyllene oxide, while Barton later established the caryophyllene formula. In his recent work, Treibs investigated the structure of Guiana sandalwood oil. Jeancard and Satie isolated a component which they considered to be a tertiary alcohol and called "maroniol." In his systematic investigation, Treibs now found that not a tertiary alcohol but rather a dioxide $C_{15}H_{22}O_{22}$ is present. The purification of the dioxide is only possible by chromatography, not by distillation. Hydrogenation of the dioxide revealed the presence of a double bond, as two hydrogen atoms were absorbed. Ozonization, separating formaldehyde and yielding a dioxidoketone $C_{14}H_{20}O_3$, showed that the double bond must exist in a methylene side chain. Sabetay's azulene reaction was positive. Dehydrogenation with selenium yielded guaiazulene. Treibs is of the opinion that similar sesquiterpene oxides will be found in many essential oils.

Once more it has been shown that the chemistry of essential oils is far from being settled. Although sesquiterpenes, due to their faint odor, have only slight importance for perfumery, interesting perfume bodies can certainly be expected to be found amongst their derivatives. These unknown compounds might even offer the key for the synthesis of many essential oils—*Dragoco Report*.

Orange Oil

The essential oils of citrus fruits are located in oil sacs or glands ranging from 0.4 to 0.6 mm. in diameter at irregular depths in the flavedo or outer rind of the fruit. These receptacles are surrounded by the debris of degraded tissue and are not connected to the surroundings. The oils are chiefly made up of terpenes. Approximately 90 per cent of the oil from oranges is *d*-limonene.

The oil may be removed from the peel either by cold pressing or distillation. In addition, oil is centrifugally removed from the oil liquor from the extractors which press the whole fruit. It is noted, however, that cold pressed oil is the most important and the only one admitted by the U. S. Pharmacopoeia.

In one procedure, peel from the reamer extractors is conveyed to double-screw presses which lacerate and twist the peel causing the oil to be released from the flavedo. Water sprayed on the screen of the press picks up the oil in a one per cent emulsion. Orange peel typically contains 12 pounds of oil per ton of oranges; about one-third of which is pressed out in this operation. The oil undergoes refinement in three stages: First, the emulsion is broken down in a centrifuge, the discharge from which is 15 to 30 per cent oil. The oil cream passes to a bowl centrifuge which yield a 99 per cent oil discharge. Most of the remaining moisture is removed by a third, continuous centrifugal separator which yields an orange oil of greater than 99.9 per cent purity. After refrigeration, at 0° F., the oil is again centrifuged to remove small amounts of stearoptene, the waxy portion of the oil.

The major use of cold pressed oil is in food industries where the flavor of the orange is desired. It is also added to beverage base products. It may be concentrated by vacuum distillation to reduce the limonene content from about 90 to 50 per cent for use in beverage products.

Distilled oil is recovered from the impure effluent of separators used in purifying cold pressed oil. The various discharged contain approximately 0.1 per cent oil. It is distilled in a steam-box still, containing baffles which guide the direction of flow. The vapor goes through a water-cooled condenser and the water and oil are collected in a drum. The distilled orange oil is decanted from the top of the drum. This

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oil undergoes further refinement through centrifuging, and the product is used in perfumes and soaps.

Almond Flower Oil

Extraction of the flowers of the almond tree with petroleum ether gave 0.0128 to 0.0135 per cent of a wax-like concrete essence from which alcohol extracted 42 per cent of a syrupy absolute essence. Distillation of this material with superheated steam gave 12 per cent of essence. The phenols and free acid were removed with three per cent sodium hydroxide solution, from which the phenols, cresol and eugenol were precipitated with carbon dioxide. Caproic and phenylacetic acids were isolated. On saponification with one per cent of alcoholic potassium hydroxide, the neutral part of the essence gave 1-decanol, geraniol and phenylethyl ether. Acetic acid was the only combined acid.

Maple Flavor

Since our knowledge of the natural components of maple is very vague, according to *The Giraudan Flavorist*, and the use of natural maple for all maple flavored products is impractical and uneconomical, what do we use for maple flavoring? For a good many years flavors based on extracts of foenugreek have been used to flavor syrups or other products normally maple flavored, such as candy, ice cream, baked goods and tobacco. These flavors have become so well known that, although different from natural maple, they are preferred by some consumers to the natural product. Most consumers, however, still prefer the natural product.

The seed of foenugreek which is grown in India, Persia, Arabia and Greece is used to make the flavoring extract. The flavor of this plant is reminiscent of celery with an extremely tenacious musty-green character. Although the flavor will vary to a certain extent with the manner in which foenugreek seed is processed, there is no similarity in structure between the plant and maple trees and no similarity in processing conditions between the extraction of foenugreek flavor and the preparation of maple syrup.

On the other hand, one of the aromatics which has found increasing use in maple flavors, is a pure synthetic cyclic ketone sold under various trade names. Although not specifically identified in maple, its odor and flavor are more characteristic of maple, especially in the hands of a trained flavorist. It is combined in maple flavors with other aromatics that are natural to wood products and also reaction products of the type that take place in the typical browning reactions. Research on the type of reaction responsible for maple flavor and the newer aromatics made available by the aromatic research chemist enable the present day flavorist to use the same artistry to produce maple flavors of greater fidelity.

The dynamic nature of imitation flavor production has its counterpart in the natural product. Work done at the Eastern Regional Research Laboratory on maple has resulted in increasing the flavor of maple syrup four to six times by determining the optimum processing conditions for flavor development.

Resinoids

The odorous properties and concentrations of resinoids vary according to the manufacturing process. Thus, the benzene extract of castoreum smells stronger than the resinoid made with alcohol, while the resinoid of oak moss made from the alcoholic extract smells much better than the one from the benzene extract. Other products are obtained from the petroleum ether extracts. In almost all cases, removal of color also causes some changes of odor. Purified resinoids are superior to their corresponding essential oils in quality of odor and concentration. In contrast to many essential oils, resinoids have no terpenous or camphoraceous note which appears during steam distillation of the drugs.

Janistyn warns against adulteration and the "pseudo-resinoids" consisting of high-boiling resinous solvents, artificial resin esters and containing none or a very modest addition of true resinoids. In most cases they contain essential oils or aromatics to substitute the odor of the resinoid. The proportion of resinoids in a composition requires careful consideration not only because resinous fixatives are specific for certain odors, but also because of the fact that too large a quantity can be detrimental, while a small one might be without effect. Experienced perfumers often limit the use of resinoids or do without them altogether because of the following disadvantages inherent in these compounds: (1) Modern perfumes containing 12 to 18 per cent aromatics require appreciable quantities of resinoids. The trend is towards only faintly colored perfumes, but even the de-colored resinoids cause perceptible coloration. (2) Some resinoids assist the "souring" of perfumes or are the actual cause. In particular, these are products containing benzoic acid, cinnamic acid or unstable resin complexes. (3) Nearly all resinoids reduce the development of the fragrance. (4) Spots on clothing made by perfume with resinoids are even more difficult to remove.

However, their disadvantages are less conspicuous in soap essences, where they can be used in large quantities, although discoloration must be watched.

Taste Sensitivity

Taste panels can spot an 0.04 per cent saline solution, which amounts to one tablespoonful of salt in 10 gallons of water. One tablespoonful of sugar in two gallons of water, or 0.2 per cent, has a sweet taste. The sour taste of acid, using concentrated hydrochloric acid, can be detected when one tablespoonful is dissolved in 40 gallons of water. The bitter taste of quinine is strongest of all, one tablespoonful in 1000 gallons of water being detected.

Palmarosa Oil

Until recently, the world's supply of palmorosa oil has been produced in India, the oils being distilled from the wild plants. During the last 20 years, however, palmarosa grass has been grown successfully in the Seychelles from seeds obtained from India. Palmarosa oil was formerly used largely as an adulterant of Bulgarian or Turkish Rose oil. It is now the source of a very high grade of geraniol. It is also widely used in cosmetics, in soap perfumes, and in the flavoring of tobacco.

Stabilizing Lemon Oil

In a study of the stabilization of lemon oils by antioxidants, dihydronorguaiaretic acid 0.01-0.04, propyl gallate 0.01-0.04, and ethyl gallate 0.01-0.04 per cent gave good results in preserving lemon oils from citral oxidation for 30 to 120 days. The use of alpha tocopherol was not satisfactory.

Removing the closure from bottles or carboys containing citrus oils permits the air to enter, resulting in oxidation of unsaturated oil constituents, with the production of sharp, bitter flavors. The more often the closure is removed, the greater the deterioration.

It is easy to prevent this oxidation, however, by the following procedure: drop a small piece of dry ice into the container before closing. Carbon dioxide gas will form a protective blanket.

Skin Research

Antifungal Butylphenylsalicylamide

From a series of substituted salicyalamides synthesized by Jules, *et al.* and screened for antifungal activity by Hok and Pilcher, N-*n*-butyl-3-phenylsalicylamide emerged as the most potent compound in the group in its activity against *Trichophyton mentagrophytes*. Inhibition of growth of this organism was brought about by a concentration of 1:512,000 in Sabouraud's agar and 1:64,000 in the presence of serum. The compound also showed a high order of activity against *Microsporum audouini*, the causative agent of tinea capitis (ringworm of the scalp). Salicylic acid is known to be mildly irritating and salicylanilide must be restricted in its use as a topical antifungal agent because of potential irritant effects on the skin. It was, therefore, deemed necessary to establish some parameters of toxicity and skin irritant properties of this related compound in animals before investigating its possible value as a therapeutic agent in man.

The compound was found by V. P. Seeberget al. (*J. Am. Pharm. Assoc. Sci. Ed.* 45:342, 1956) to possess a low order of systemic toxicity. No evidence of topical irritation or toxicity could be evoked by repeated application or relatively large amounts of the compound to young rabbits. The compound is only slightly absorbed orally. By administration in a special vehicle consisting of 25 per cent Tween 80, 25 per cent propylene glycol and 50 per cent water, absorption of approximately two per cent of an oral dose was obtained.

Skin Penetration— Guillot and Valette

Water - soluble non - electrolytes. Few water-soluble organic substances can be easily absorbed by the skin. With dyes, Aoki obtained only negative results with acid dyes (fuchsine S, indigo carmine) and with basic dyes (rhodamine B, trypaflavine). Applied to the skin of a rabbit, in aqueous solution, dissolved in alcohol or as an oily emulsion, these substances do not appear in appreciable amounts in the urine. Nevertheless, after treatment of the skin with soap solutions or volatile solvents (gasoline, petroleum ether), a fragment of live skin is penetrated by these dyes.

On the other hand, Imschenetzsky has noted that in the rabbit prolonged contact of the skin with an aqueous solution of trypan blue is followed by exudative inflammation accompanied by alteration of the epithelium and the follicles. This superficial lesion creates a "doorway" which allows the dye to reach the lymphatic vessels. Application of the dye without pressure leads only to accumulation in the superficial cornified layer, from which it can be concluded that there is no absorption of water-soluble dye by the intact skin.

In the case of antigens, application of diphtheria toxin to the intact skin of the guinea pig or rabbit after previous treatment with ether causes the death of the animals. The results are even more striking with tetanus toxin which, without local inflammatory response causes a typical case of tetanus in the guinea pig.

Golowanoff and Walter used a sensitization reaction to demonstrate penetration through the skin of the proteins of cottonseed and peanut. The subject is sensitized by several successive injections of serum from individuals who show a cutaneous reaction to the antigen. After this passive sensitization, the same antigen is applied to the skin, penetration being proven by the development of a wheal.

From these results it is possible to conclude that certain water-soluble substances may penetrate the intact skin, at least in traces. It is possible that the affinity of these antigens and toxins for certain constituents of the tissues is the cause of their absorption; we must note, however, that cleansing of the cutaneous surface is a necessary condition for the penetration of these substances.

Stejskal reported that it was possible to make sugars and proteins penetrate the skin to such an extent as to bring about appreciable nutritional effect by the cutaneous route. These very surprising observations were not confirmed by Winternitz and Naumann, nor by Baucke, at least as concerns penetration of the skin by sugars.

Essential oils and their constituents. The penetration of essential oils through the skin has been demonstrated by Paffrath in the case of a mixture of thyme, eucalyptus, turpentine and cypress by identification of constituents of the mixture in expired air; elimination through the lungs takes place 24 hours after application to the skin and is more intense than urinary elimination. Macht, in his systematic studies with different animals, noted that most of the essential oils applied to the skin caused definite pharmacological reactions, characterized either by a period of excitement followed by depression, or by immediate depression. Used in high doses, all essential oils appeared to be toxic. On autopsy, animals showed lesions of the kidneys and the central nervous system. Peppermint, thyme, jasmin and tansy oils appeared to be the most toxic. Continuing his experiments with constituents of the oils, the same author noted the effects of safrol, isosafrol, fenchyl alcohol and menthol. Macht has also shown that these oils and their constituents can be utilized as vehicles for the introduction of alkaloids. When these solutions were applied to the skin of animals, the latter showed pharmacological reactions that gave proof of the penetration of the active substance.

Valette has sought to make Macht's results quantitative by determining in the rabbit the speed of penetration of various oils and their definite chemical principles. Maximum speed was observed with oils of turpentine, thyme, eucalyptus, alpha pinene, eucalyptol, linalyl and geranyl acetates. These results were confirmed in mice by using

the liquid as solvents for aconitine and determining the time for the preparation to cause death after application to the skin.

Organic solvents. Because of what we know concerning the importance of liposolubility in percutaneous absorption, it is not surprising that organic solvents have a very high skin-penetrating power.

Parisot noted that ether and chloroform rapidly traversed the epidermis; solutions of atropine in these solvents when applied to the skin of the forehead of human beings caused dilation of the pupils in a few minutes; with alcohol, this action was evident only after the elapse of at least one-half hour. These results were not confirmed by Rohrig.

Winternitz performed various experiments on rabbits and human beings. The application of a 10 per cent solution of strychnine in chloroform to the skin of a rabbit caused the death of the animal in 20 minutes; the application of chloroform, ether or alcohol, followed by the application of an aqueous solution of strychnine sulfate brought about the same result in variable times.

Tests made on human beings with alcoholic, ethereal or chloroform solutions of cocaine or atropine gave variable results, which is explainable by the difference in thickness of human and rabbit skin.

Ether and chloroform cannot exert their narcotic action by penetrating the skin because of their great volatility. According to Burgi, general anesthesia by the percutaneous route cannot be accomplished except with substance boiling higher than 80° C.; at lower boiling points the evaporation rate is too great to allow the accumulation of adequate concentrations in the blood or nerve tissue. Joachimoglu followed histologically the penetration of chloroform and other volatile chlorinated derivatives colored with malachite green. While at low dosages only the epidermis is reached, after prolonged contact the substance penetrates the hair follicles and the upper portions of the derma.

Lazarew, Brussilowskaja, Lawrow and Lipschitz have verified the cutaneous absorption of benzene and benzine by analysis of the the air expired by mice and rabbits. Acetone is also absorbed by the skin and passes in appreciable quantities into the urine, as shown by experiments of Schwenkenbecher and recently confirmed by Valdiguie and Mestre.

We may deduce from these data that the skin can be penetrated by volatile solvents. These liquids, used as vehicles, permit the cutaneous absorption of various medicinals such as alkaloids (Winternitz), or sex hormones (Zondek). Previous treatment of the skin with solvents makes possible penetration of an aqueous solution.

Valette and Cavier have made a systematic study of the cutaneous absorption of volatile liquids of different chemical series: hydrocarbons, alcohols, ethyl esters and alkyl acetates, by using a pharmacological test based on the action of eserine on the contraction of rat smooth muscle. The substances to be tested were used as vehicles for the alkaloid whose speed of penetration through the skin could be measured.

Saturated aliphatic hydrocarbons. Experiments were made with hydrocarbons ranging from C_6 (hexane) to C_{18} (octadecane). The lower compounds are the most penetrating; there was no significant difference from C_6 to C_9; the penetrating power diminished thereafter with increased molecular weight.

Among **aromatic hydrocarbons** there was little difference among those studied: toluene is more rapidly absorbed than benzene; isopropylbenzene and p-cymene penetrate better than benzene and toluene.

In the **cyclic hydrocarbon** series the introduction of a methyl or isopropyl group into the nucleus (isopropyl cyclohexane or menthane) favors absorption through the skin. The introduction of a double bond as in menthane and menthene does not modify the penetrating power.

For the **terpene** series, members studied were in the acyclic series: myrcene and allo-ocimene, in the monocyclic series: limonene and phellandrene and in the bicyclic series: alpha pinene and nopinene. All of these substances are easily absorbed by the epidermis without notable variation.

Among **saturated primary aliphatic alcohols,** the first members up to C_4 (normal butanol) do not show appreciable penetration. Absorption begins at C_5, passes through a maximum for C_7 and then rapidly decreases. However, the most easily absorbed of this series, heptanol, is less active than most of the hydrocarbons. As for the aromatic alcohols, benzyl, phenethyl and cinnamyl, these have practically no penetrating power.

With **ethyl esters** the greatest speed of penetration is shown by the C_7 compound (ethyl isovalerate). The esters of aromatic acids, ethyl benzoate, salicylate or phenylacetate are less well absorbed than aliphatic acid esters with the same number of carbon atoms.

Finally, in the series of **alkyl acetates,** maximum absorption results with C_6 and C_7 (butyl and amyl acetates).

From these results we may conclude that in the chemical series examined, the penetrating power of the compounds increases with the length of the carbon chain, reaching a maximum between C_6 and C_8. Hydrocarbons are the most penetrating and alcohols least so. Although the presence of an oxygen function reduces penetration, this effect is weakened for esters; heptane, ethyl isovalerate and amyl acetate are absorbed to an equivalent extent which is clearly greater than the absorption of heptanol.

Dicyclonine Hydrochloride

Dyclonine hydrochloride (4-*n*-butoxy-β-piperidinopropiophenone hydrochloride) has been found by H. J. Florestano and M. E. Bahler (*J. Am. Pharm. Assoc. Sci. Ed.* 45:320, 1956) to possess, in addition to its topical anesthetic properties, significant bactericidal and fungicidal activity. Self-sterilizing action manifested by preparations containing the drug was considerably enhanced upon the addition of chlorobutanol. Results of *in vitro* test employing microorganisms commonly involved in local infections indicated that the two agents in combination act synergistically.

Florinef-S Ophthalmic (Squibb) is available as an ointment or a suspension containing fludrocortisone acetate, neomycin and gramicidin. It is indicated in the treatment of inflammatory eye disorders and is available in 3.6 gram tubes with ophthalmic tip or in 5 cc. Dropper bottles.

Corticosporin Otic Drops (Burroughs Wellcome & Co.) is a sterile preparation, each cc. containing 100,000 units of polymixin B sulfate, 5 mg. of neomycin and 10 mg. of hydrocortisone, intended for the treatment of ear infections. It is available in 5 cc. bottles with a sterile dropper.

Diovac Syrup (Gray Pharmaceutical) is a solution containing dioctyl sodium sulfosuccinate and sodium benzoate intended for use as a constipation corrective. It is available in 4 oz. and 6 oz. bottles.

Cyclospasmol (Camden Chem. Co., Ltd., London) is 3,5,5-trimethylcyclohexy mandelate and is claimed to be a mild vasodilator for the safe long-term treatment of peripheral vascular disease. It is available in 100 mg. tablets in bottles of 20, 50 and 250.

(*Continued from page 75*)

sensitivity to moisture.

"The pure or substantially pure dextrans are bland, non-toxic, non-irritating substances which are more or less hydrophilic. It is said that while esters of the dextran with the fatty acids of from eight to 18 carbon atoms differ from the parent dextrans in being more or less water-resistant, they are like the dextrans in being bland, non-irritating harmless substances ideally adapted to use as the base for various types of cosmetic preparations."

The degree of substitution (D. S.) or the average number of fatty acid radicals per anhydroglucopyranosidic unit of the dextran should be from less than 1.0 to 3.0.

In the words of the patent:

The ester may be selected for the particular type of cosmetic of which it is to comprise the base, alone or in admixture with other adjuvants including inert fillers and conventional waxes and oils. Thus, those esters having a D. S. from about 2.5 to 3.0 and derived from fatty acids containing from 14 to 18 carbon atoms are water-repellent substances of wax-like consistency. These water-repellent esters are particularly suited to use as the base of compositions for use as cheek rouge or molding into lipsticks. They are remarkably adherent to the skin. For instance if a film of a dextran palmitate or of a dextran stearate containing an average of 2.9 palmitoyl or stearoyl radicals per anhydroglucopyranosidic unit forms on the hands during handling of dispersions or solutions of those esters, the film is not removed by vigorous scrubbing with soap and water. Used as the base or binder for cosmetic preparations, these water-repellent, wax-like dextran fatty acid esters, yield products which have excellent hardness at normal temperature extremes, rub off readily when applied to the skin, and exhibit good staying power on the skin. These esters may also be used as the base for so-called "solid" perfumes such as perfume sticks comprising essential perfume oils.

On the other hand, the dextran esters of lower D. S., i.e., those containing an average of from less than 1.0 up to about 2.0 of the fatty acid radicals per anhydroglucopyranosidic unit, are preferred for use as base component for other types of cosmetic products such as creams, shampoos, and similar products and in which the dextran ester functions as a base or binder and may also serve as a suspending agent.

The proportion of dextran ester used in the compositions is usually from 30 per cent to 50 per cent of the total.

All of the claims specify lipsticks and claim 1 is reproduced here:

A lipstick comprising coloring matter and a base comprising an ester of a dextran with a saturated fatty acid of from 14 to 18 carbon atoms, said ester containing an average of from 2.5 to 3.0 of the fatty acid radicals per anhydroglucopyranosidic unit.

U. S. 2,749,277 deals with the use of dextran in liquid or dry powder compositions used for tinting the skin. The preparation is tinted in accordance with the particular area of the skin to be coated, the tinting being different for preparations to be applied to the face than for preparations intended for use in leg make-up or the like. According to the patent, the compositions when applied to skin provide it with a surface finish or coating which is smooth and firmly adherent, resistant to streaking, stripping off or roughening and which is non-toxic, non-irritating and does not cause harmful effects if it comes in contact with lesions or open cuts.

The key to the novel preparations is that they comprise particles of body powder carrying a protective film of dextran which is said to produce a powder preparation of substantial adhesiveness and which provides a film coating over the entire powdered surface so that in effect the powdered area is provided with a continuous, protective dextran coating.

The following example, taken from the patent, shows the preparation of a "pancake" type composition:

About 5.0 ounces of a pure dextran having an average molecular weight of about 70,000 to 85,000 is dissolved in water. About 10 ounces of a mixture of approximately equal parts of talc, zinc oxide and calcium carbonate are blended with the dextran solution. The mixture is then dried and granulated to obtain a mass of fine particles which carry a film or coating of the dextran. The mass is compressed in the usual way to obtain a preparation of the so-called "pancake" make-up type, adapted to be moistened, picked up on a sponge and applied to the face to provide it with a firmly adherent, mat-like protective and concealing finish.

RECENT PATENTS

2,743,276—**F. E. Anderson—(2, 2-Dimethyl-3-Hydroxy-propylidene-1) Hydrazone of Isonicotinic Acid Hydrazide.**

2,743,287—**Ciba—Hydroxyl Compounds of the Steroid Series.**

2,743,294—**Akt. Pharmacia (Sweden)—Bis-Alkylammonium Ethers.**

2,744,048—**Allied Labs.—Substituted Alkyl-Diphenyl-methane Anthelmintic Compositions.**

2,744,049—**Colgate-Palmolive—Stabilized Dental Creams.**

2,744,108-9-15—**G. D. Searle—3-Ethylene Mercaptoles Derivatives of Pregnenes.**

2,744,112—**Hoffmann-La Roche—Optically Active**

(*Continued on page 134*)

Trade Literature

Whittaker's Cosmetic Materials

Whittaker, Clark & Daniels, Inc., 260 West Broadway, New York 13, have issued a 214-page book entitled "Whittaker's Cosmetic Materials." This spiral-bound book, known as Bulletin No. 56-1, gives full specifications on the extremely wide range of cosmetic materials which the firm handles. In addition much information on the use of many of these materials is given. The book is divided into three parts. Part I covers the inerts (non-metallic minerals) and light chemicals, including talcs, kaolins, calcium carbonates, stearates and similar products. Part II treats with Whittaker-Thomasset D&C colors for cosmetics. Part III is a cross reference by use. The company explains: "It is impossible to pin-point the exact usage of these materials because of the many personal preferences of individuals and the varied types of products in which they will be used. Since there is overlapping of many basic materials used for various products, it is often difficult to explain why one particular material should be selected."

Morningstar—Paisley

Available from Paisley Products, Inc., for the past 25 years, a division of Morningstar, Nicol, Inc., 630 West 51 Street, New York 19, is a 20-page, two-color, illustrated booklet describing the Morningstar products and their applications in various industries—including drugs, pharmaceutical, and cosmetic industries—as well as the Paisley adhesives and their applications in the packaging and shipping operations of the same industries.

Nadone (Cyclohexanone)

National Aniline Division, Allied Chemical & Dye Corporation, 40 Rector Street, New York 6, has issued Technical Bulletin 1 to 19 on Nadone (cyclohexanone). This 32-page bulletin contains what is believed to be the most complete data yet to be assembled on this unusual solvent and chemical intermediate. It contains 17 pages describing physical and chemical properties, and describes and illustrates all principal reactions. It also provides seven pages of suggested uses.

Groco Fatty Acids

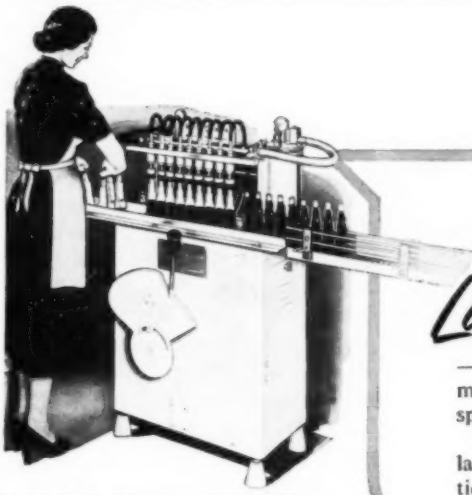
A four-page brochure tabulating the specifications and components of Groco fatty acids has been issued by A. Gross & Company, 295 Madison Avenue, New York 17. The brochure permits the reader to see at a glance all vital data, as well as distributors throughout the country.

Epoxy Compounds

Becco Chemical Division, Food Machinery and Chemical Corporation, Buffalo 7, N. Y. has issued Bulletins, Nos. 72, 73 and 74, which respectively describe Becco's new long-chain epoxidized olefins, octylene oxide, dodecene oxide, and C_{16}-C_{18} olefin oxide. Structure, typical properties, and chemical reactivity of each of these highly reactive epoxy compounds are presented.

Peoples Drug Store

To Make A Business Grow is the title of a six-page brochure telling the story of why the Peoples Drug Store grew from a single small unit in Washington, D. C., in 1905 to a 158-unit business doing more than $57 million annual volume in 38 markets. The story is told by the Bureau of Advertising, American Newspaper Publishers Association, 570 Lexington Avenue, New York 22.



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trol of air velocity. Conjointly with this system, there must be air exhaust with a suction greater than the force of the air so that dust can be removed and contamination of other tablets in the work area avoided. The preparation of syrups is best done in steam-jacketed kettles because excessive heating will darken the solutions. Convenient work benches, racks and trays for storage of tablets in process, accurate scales, screens for removal of dust and broken pieces are all essential items. It is advisable to isolate the polishing area from the coating section.

Stephenson and Smith[20A] analyzed the coatings of a number of tablets and found that 51 to 91.6 per cent of their ingredients were water soluble, with sucrose comprising almost the entire amount. On the basis of this information they proposed that sucrose be present in a minimum of 50 per cent to insure rapid disintegration of the coating. Such a standard might run afoul of efforts to shorten and improve the coating process as indicated by the work of Gans and Chavkin.[13] Stating that pan coating required about three days and ateempts to decrease the time by varying present techniques were unsuccessful, they proposed the use of polyethylene glycol 6000. Using a small coating pan they applied the coating in alcohol at concentrations of 25 to 50 per cent. Build-up was rapid, the tablets drying quickly between coats. According to the authors light and dark colors were applied with equal facility and success. The use of alcohol as the solvent eliminated water-proofing of hygroscopic tablets.

Another method for shortening the coating time is to speed up the drying interval. Pitman-Moore of Indianapolis have used infrared drying in coating pans for products not affected by that type of heat. Drying time of the subcoat was reduced one-third and the residual moisture content from two to three per cent to one to two per cent.

A facet of coating which has received a great deal of attention is enteric coating. It has been stated that a good enteric coating will stand up in the stomach indefinitely but will rupture or disintegrate withine one hour in the intestine.[18] It should resist mechanical trauma and not act as a semi-permeable membrane. It should, of course, be non-toxic and its decomposition products, if any, will be equally harmless.

Many enteric coatings depend upon the difference in pH between the stomach and the intestines and are chosen, therefore, because of their insolubility in acid media and solubility in alkaline media. However, the duodenum frequently has an acid reaction and the coating may not dissolve there. Other substances have been chosen because they are saponifiable by lipase enzymes but are undigested by the stomach. A third group consists of hydrophilic vegetable substances which swell in the presence of moisture regardless of pH, and therefore, have "timed" disintegration postulated on the rate of swelling.

Keratin, an albuminoid, supposedly insoluble in gastric or pancreatic juices was one of the earliest substances used as an enteric coating. However, Goorley and Lee later demonstrated that it actually was soluble.[7] For a time salol, that is phenyl salicylate, was much in favor but it forms an uneven coating, has a low melting point and cracks readily. Salol when used alone has a maximum disintegration time of two hours in man but when combined with bleached shellac resists artificial gastric fluid for about five hours and artificial intestinal fluid for two to three hours.[14] Zein, a gluten derivative, was tested by Couvreur. Working on a semi-commercial scale, he found the material difficult to work out and, in addition, he found the coating fragile and ineffective.

Shellac has been used alone and combined with many other substances. According to Couvreur, when sufficient coats are applied to resist gastric fluid, the tablets also resist intestinal fluid for too long a period.[23] On the other hand, a study in the United States on rats revealed satisfactory results.[25]

Other resins such as benzoin, tolu, sandarac and mastic have also been used, but there is little scientific support for their use. Cetyl alcohol with mastic gave no protection even after forty coats. When cetyl alcohol was combined with sandarac and the tablets coated alternately with it and with balsam tolu, the resistance to gastric fluid was satisfactory. Unfortunately, intestinal fluid was also unable to break down the coating.[23]

Another approach to enteric coating has been the utilization of fats and fatty acids. Of all food components ingested only fats pass through the stomach unaffected with saponification taking place in the intestine. Therefore, fats should make an ideal enteric coating. However, fats are soft and melt at comparatively low temperatures so that they fail to resist digestive abrasion and body heat. An interesting formulation developed at the University of Iowa uses myristic acid as the fatty acid providing firmness with hydrogenated castor oil promoting elasticity. Cholesterol is added to increase emulsifiability and sodium taurocholate to promote disintegration in the intestine. Variations in the latter two ingredients alter the timing of disintegration. One investigator found the composition resisted gastric fluid for over ten hours.[28] Another showed that some tablets left the stomach in two hours to disintegrate in one-half hour in the intestines, while others passed into the stomach after six hours to disintegrate in two hours in the intestine.[19]

The DANISH PHARMACOPOEIA of 1948[23] recommended a formula containing small quantities of vanillin, terpineol, monoleinum—a mixture of the glycerides of oleic and other fatty acids—and a large amount of shellac. Thirty applications gave very satisfactory results, although the actual coating with it was not easy. After six months storage, however, the

(Continued on page 120)

Industry's Books...

Medicinal Chemistry, *Vol. II, 307 pp., John Wiley & Sons, Inc., New York (1956), cloth,* **$10.**

This is a series of reviews prepared under the auspices of the Division of Medicinal Chemistry of the American Chemical Society. Contents include: 1—Some Chemical Aspects of the Cardiac Glycosides, Arthur Stoll—Supplement, T. L. Johnson. 2—Synthetic Estrogens, John A. Hogg and Jerome Korman. 3—Analgesics. Arylpiperidine Derivatives, C. M. Suter. 4—b-Haloethylamine Adrenergic Blocking Agents; Chemistry and Structure-Activity Relationships, Glenn E. Ullyot and James F. Kerwin. Index.

Fundamentals of Selling the Supermarkets, *by Julian H. Handler, Editor, Supermarket News, 159 pp., Illus., Fairchild Publications, Inc., (1956), cloth,* **$5.**

This is a comprehensive book on the merchandising of non-food products in the supermarkets. The book was planned as a guide for manufacturers and distributors in considering and developing opportunities for marketing their non-food lines through large food outlets. The author describes the different methods used in merchandising non-food items, as well as the factors that manufacturers should consider in deciding whether their products are adaptable for this field.

Plant Physiology, *by Meirion Thomas, M.A., F.R.S., Professor of Botany at King's College, Newcastle upon Tyne, with the collaboration of S.L. Ranson, B.Sc., and J. A. Richardson, M.Sc., Fourth Ed., Illus., Philosophical Library, New York, (1956), cloth* **$12.**

In this new edition the most extensive changes will be found in the chapters dealing with enzymes, respiration, and photosynthesis, and in scattered sections dealing with the absorption of water and solutes, transpiration, stomatal movement, Crassulacean acid metabolism, cell growth, and auxins. A completely new chapter reports facts and views about photoperiodism and vernalization and an appendix has been added describing those techniques used in partition chromatography and in experiments with isotopic tracers which have led to some of the developments reported in the main body of the book.

Essentials of Dermatology, *by Norman Tobias, M.D., Dermatologist, St. Louis State Hospital, Fifth Ed., Illus., 651 pp., J. B. Lippincott Co., Phila., (1956), cloth,* **$8.**

Every one of the more common dermatoses is concisely and authoritatively described and discussed. Full descriptions of those drugs which may produce eruptions are included. Material is especially ample on the subject of contact dermatoses in children; tables of localization and contact causes have been provided for rapid pinpointing of these problems. Seven new full-color illustrations have been added to those appearing in former editions of the text.

The Care of Your Skin, *by Herbert Lawrence, M.D., 95 pp., Illus., Little, Brown and Co., Boston, (1956), cloth,* **$2.50.**

This book is devoted almost entirely to acne, an ailment which is very prevalent, particularly in adolescents. It is written for the layman and tells how to treat acne and how to overcome it. The basic object, says Dr. Lawrence, is to remove excess oil from the skin. Dr. Lawrence tells how to do this and gives complete information on proper cleansing, correct diet and exercise. He also describes the specific beneficial treatments provided by dermatologists.

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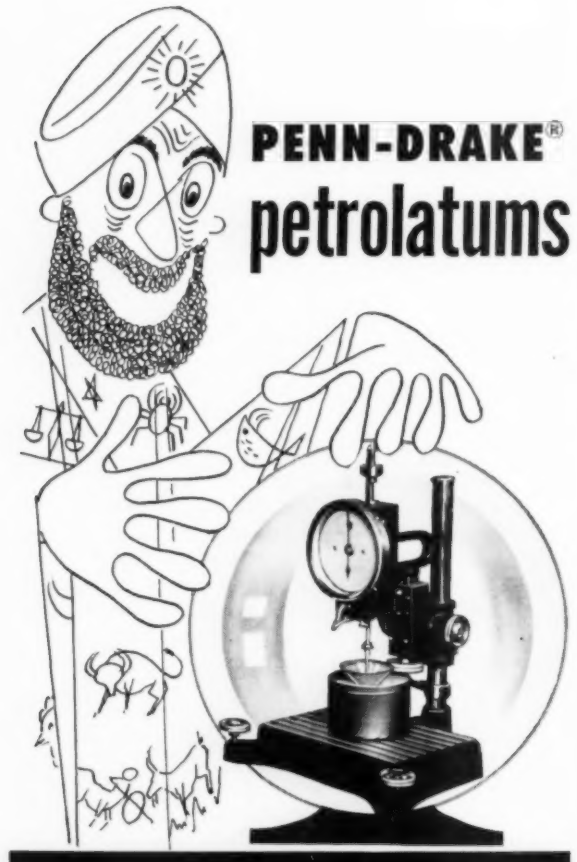

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(Continued from page 118)

tablets remained whole after two hours in intestinal fluid with a pH of 6.9.

An enteric coating which has received a great deal of attention is cellulose acetate phthalate. Using capsules and tablets coated with this substance, Hodge[29] found, radiographically, that 79 to 100 per cent of them disintegrated within eight hours. The site of the disintegration was almost always the intestine. In vitro studies revealed resistance to gastric juice for as long as twenty-four hours, yet yielding to intestinal fluid in thirty to ninety minutes. Confirmation of this experiment has been given by Couvreur. Similar data were obtained by Bauer and Masucci.[30] They used tablets of sodium salicylate and tested the urine of their subjects with ferric chloride for its reaction with the drug.

In another test[32] tablets coated with cellulose acetate phthalate were selected on the basis of their efficiency as measured radiographically for comparison with a commercial batch of tablets enteric coated for timed release. Both sets of tablets were tested in eleven different artificial gastric juices for one, two and three hours, and the loss in weight calculated. They were then tested in twelve artificial intestinal fluids and the time of disintegration determined. They were also tested in the stomachs and intestines of rats. The former tablets had better protection from acid attack and disintegrated better in the pancreatic juices.

Several cellulose derivatives were evaluated for their enteric properties by Antonides and DeKay.[33] Cellulose acetate phthalate gave excellent results but the others were either useless or only fair. On the other hand, some criticism has been leveled at this material. Kanig[18] and others have discovered that the coating is permeable to the test fluids. Sodium chloride tablets, for example, leached out, although the coating remained whole. Smith, Kline and French have secured a patent covering the use of several waxes and glyceryl esters as additional coatings to overcome this weakness. The Columbia University College of Pharmacy made a solution combining 15 per cent cellulose acetate phthalate with 10 per cent hydroabityl alcohol. The coating withstood the attack of artificial gastric fluid for 5½ hours yet disintegrated within 40 minutes in intestinal fluids whose pH ranged from 6.9 to 8.4.

Not to be overlooked in considering the efficacy of an enteric coating is the material used to prevent tablets from clinging together or to the pan as the enteric coating passes through the "tacky" stage. Bukey and Klemme[34] investigated the efficiency of mastic dissolved in methyl propyl ketone when dusted with talcum or magnesium stearate. Using pills of barium sulfate, they found that 49.5 per cent of those coated with mastic-talcum disintegrated in the intestine whereas 62.5 per cent of the mastic-magnesium stearate pills disintegrated there. Seven point five per cent of the former broke down in the stomach while

30 per cent of the latter did so. Fifty subjects were involved in this test. A much larger project was undertaken by Hawkins and Thompson.[35] They used three different types of enteric coatings and 14 conspergents. The protective coatings were:

1. Stearic acid, mutton tallow, balsom tolu and sodium taurocholate.
3. Shellac.
2. Cetyl alcohol, sandarac tolu.

The authors concluded that the efficiency of any coating was not entirely a function of its thickness. Magnesium stearate, calcium stearate, talcum and aluminum palmitate were the best dusters, the observation of Bukey and Klemme being confirmed in regard to talcum and magnesium stearate. All four worked well with shellac; calcium stearate was the best with the other two formulas.

As varied as are formulas for providing enteric coatings, the methods for testing them are almost as numerous. "In vitro," there has been no consistency in apparatus, composition of test media, temperature, methods of agitation (if used) or end points. "In vivo," tests have ranged from observing the action of the drug on the subject to x-ray. Some investigators postulate the disappearance of the tablet through a screen while others are satisfied if the core becomes mushy. Brindamon and DeKay[32] tested two sets of tablets in eleven different gastric juices and twelve different intestinal fluids. In some cases, the tablets used in the gastric portion of the test are transferred to the intestinal fluid; in others, fresh tablets are used in the second juice. The need for standardization is obvious. However, great care is essential, for it appears likely that different coatings act differently in different media and apparatus. Hence, the various formulas should not be evaluated according to the results of an in vitro test but rather according to the correlation between such a test and a selected "in vivo" examination.

One aspect of enteric coating which seems to have been neglected in setting up tests is the trend toward delayed action, repeat action and sustained action tablets. Here release of the drug is desired at a fixed interval or at a regular rate regardless of the position of the tablet in the gastrointestinal tract. The coating must not be impervious to gastric juice for an unlimited time nor soluble in the pancreatic fluid in a brief time.

The idea of protecting tablets from moisture has been applied in a mild form. Plain tablets have been coated with a few coats of film so that monograms and score markings will remain clear. A patent[37] has been issued for the use of silicone resins such as Dow 803 and 804 and General Electric 9980. Capsules so coated resist separation of their component parts. Gaseous silicones may also be used, except that the gloss is less.

Cellulosic high polymers have more recently been advocated for this purpose.[38] On a laboratory scale,

(Continued on page 124)

SOUTHERN COMFORT U. S. A.

BY JOHN HARDER, WRITER

RECENTLY I visited the Southern headquarters of Knox Glass, Inc., in Jackson, Mississippi . . . and the welcome was one of real, old-time Southern hospitality. From their *"on their toes"* attitude—you'd never in the world know you were in "a bit of the ole S'uth." *Modern production facilities, a live sales and service organization, and long time employee service furnish the backdrop of this operation.* Whether it's Knox *South* or Knox *North,* you'll find comfort in the quality of this Company's glass containers — and their service. There are seven plants (soon there will be eight) and many, many sales offices all over the good U.S.A. Call Knox!

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Readers' Questions . . .

Baby Lotion: *We would like very much receiving from you information concerning a formula for a modern type baby lotion.* MUNICH.

A baby lotion must be as nearly non-irritating as possible and ingredients must be selected with this always in mind. Mineral oil, enhanced by silicone, is a satisfactory protective agent; the emulsification system consists of non-emulsifying grade glyceryl monostearate and a suitable non-ionic along with a cationic for antibacterial activity. The pH of the system should be buffered to value in the neighborhood of 5. A formula for preliminary work is the following:

Mineral oil	10.0
Silicone	1.5
Glyceryl monostearate	2.0
Sorbitan monooleate	0.6
Benzalkonium chloride	0.1
Glycerin	3.5
Perfume	0.3
Water	82.0

Hand Cream: *Can you supply me with a formula for a hand cream containing a large proportion of glycerin and some lanolin? Is there an agent used in creams to aid the absorption of emollients such as lanolin? Is there are reason for the inclusion of vitamin C in cosmetic creams.* SEATTLE.

A formula for a product with your ingredients is the following:

Glyceryl monostearate	12.0
Lanolin	2.0
Mineral oil	1.0
Glycerin	10.0
Methyl paraben	0.1
Perfume	0.4
Water	74.5

The absorption by the skin of various substances including emollients is largely dependent upon the properties of the compound to be absorbed and may be related to a ratio between water-solubility and oil-solubility. There is no ingredient that can be added to the cream to improve the absorbability of the components. I do not believe that ascorbic acid serves any useful purpose in cosmetic creams; in most formulations it would be quickly oxidized, losing vitamin value and causing discoloration.

Preservative: *Our product is a cosmetic cream containing vitamins, 10 to 15 per cent of vegetable oils and has a pH value of 5. Can*

you suggest a suitable mold preservative for you suggest a suitable mold preservative for this type of product that will be effective over a long period of time? LOS ANGELES.

A combination of parabens, 0.18 per cent of methyl paraben with 0.02 per cent of propyl paraben, is highly effective as a preservative. Sodium benzoate, at low pH values, is effective and may also be used in combination with the parabens. I would suggest the inclusion of an antioxidant, butylated hydroxyanisole, to protect the vegetable oils from rancidity.

Dandruff Preparation: *Would it be possible in our dandruff preparation to include hexachlorophene or allantoin along with the resorcinol we now use? Are any other ingredients useful in treating dandruff?* NEW YORK.

I contemplate no incompatibility between hexachlorophene and resorcinol or allantoin and resorcinol. Sulfacetimide as well as a complex sulfur compound, Vancide, have been reported as being effective in the treatment of dandruff; the addition of quaternary anti-bacterial agent might also be useful.

Stannous Fluoride: *We have been asked to supply stannous fluoride. Do you know of any commercial source for this material?* SALEM.

We are not aware of a source of supply for this material. Offhand, it should be easily made by double decomposition between stannous chloride and sodium fluoride, since it is reported to be sparingly soluble, but the degree of hydration may be important in determining its suitability for dentifrice use and it may form less useful double salts when manufactured by ordinary means.

Non-oily Hair Lotion: *In formulating a lotion for the scalp, containing ingredients for the treatment of seborrheic dermatitis, what agent or group of suspending agents would you recommend? I wish to avoid the use of oils and fatty substances yet would like to have a preparation that would keep the hair in place.* ROCHESTER.

You might do well to look into the formulation suggestions made in a recent article on "Suspensions" in this magazine. Mixtures of a gum such as one of the algins, methyl cellulose, sodium carboxymethylcellulose, etc. with a modified bentonite will give you a suspending vehicle that can vary in consistency from a thin lotion to a thick paste, depending upon proportions, yet without oil or fat. This mixture should be reasonably effective in hair grooming, but a proportion of glycerin should be present to retard the formation of a flaky deposit.

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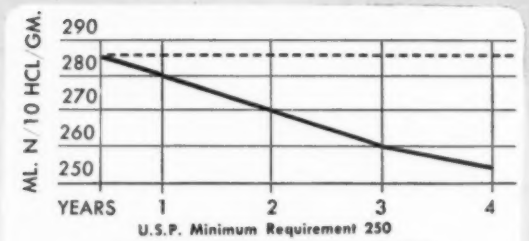

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(*Continued from page 121*)

the actual coating time is reduced to 1½ hours and the processing time to eight hours. The solutions may be colored to give further distinction to the product. Stability tests show that the coating gives protection during handling and transportation, the odor and taste of the original tablet are concealed and resistance to high humidity and heat is much better than sucrose. Most recently zein in 91 per cent isopropanol has been recommended for the same purpose.[39] The same advantages are claimed for it as for the celluloses; in addition, the shellac undercoating is not required.

(To be concluded)

THE SPHERE OF RESEARCH

(*Continued from page 41*)

not know why some substances can be applied repeatedly to the skin without ill effects, while others, not widely different chemically, can produce a rash when so applied.

3. The mechanism of enzyme actions. We know that most of the processes occurring in living tissues, and most of the effects of applied or ingested substances upon body tissues, are probably explicable in terms of enzyme systems. But for full explanation, we need to know more about how enzymes act. We do not know the exact configuration of any enzyme, nor what forces join it to the substance whose reaction it promotes, nor how this catalytic effect works.

Until we have adequate understanding of fundamentals such as these, workers in medicine, public health, nutrition, and cosmetology must attack their many problems empirically. They must continue to work largely in the dark, and that means a waste of time and money.

Protein-Enzyme Problem

Studies as fundamental as that of protein structure and function are too formidable, and of too wide a scope of application, to be tackled by any company or trade association. The only feasible avenue of effective attack appears to be through governmental agencies. Basic research on such problems would benefit our whole population, and would make the governmental efforts to protect public health more effective and in the long run less costly.

Twelve of the top scientists of the Food and Drug Administration's Division of Pharmacology recently wrote for publication[1] a summary of the methods now used in their laboratories for evaluating chemicals proposed for use in foods, drugs, and cosmetics. A great deal of the material deals with tests on substances taken by mouth, and therefore does not directly concern our industry, but the article provides an eloquent demonstration of what a boon adequate knowledge of protein structure and function would be.

Anyone reading the article will be impressed with the seriousness and thoroughness with which the authors approach their task of protecting public

health. He will also be impressed with the almost fantastic complexity and laboriousness of the methods that must now be used to establish safety of a substance with reasonable certainty, and with the time and expense involved. He will see how important it is that animal toxicity tests, with their multiple inherent variables and uncertainties, be supplemented by development of additional significant tests on the chemical level. This need is ably summed up by Lehman and Woodard, in the above article (p. 744): "It would be foolhardy to pretend that all possible effects in man can be predicted from the results of animal experimentation."

In the same article (p. 696) Woodard says: "At the present time, there are only a few enzyme systems for which it has been clearly established that a chemical effect has much meaning for the pharmacological or toxicological behavior of a chemical. The importance of the cholinesterase and the carbonic anhydrase systems in the evaluation of the action of chemicals is well recognized. Effects of a few chemicals upon the carbohydrate cycle would appear adequate to explain their mechanisms of action. Although the importance of a variety of other enzyme systems to the proper functioning of the body is known, it is not clear at this time how much weight can be given to the effect of a chemical on one of these systems in the evaluation of the safety of such a chemical. *Undoubtedly, the near future will see more and more emphasis given to the action of chemicals on a large variety of selected enzyme systems.*" (*Italics supplied*)

Laug (p. 703) says: "Much progress has been made in connection with tetraethyl pyrophosphate, parathion, and a host of others of like nature, because of the early discovery of their anticholinesterase action. It is a wry fact to note that in the case of DDT, even though the compound has been widely used for ten years, no such dysfunctioning enzyme system has yet been found, which fully explains the observed toxicity."

Frawley (p. 707) says: "The proper design of a subacute ['toxicity'] experiment can result only from experience, insight, ingenuity and, in some cases, serendipity. Occasionally it is possible to predict the physiological activity from structurally related compounds, and the experimental design can be based on knowledge of these compounds. However, many compounds do not permit this sage judgment at this stage of investigation. Thus we must rely on as many screening techniques as possible to detect the type of toxicological change that occurs. These techniques are still in their infancy, particularly for detecting functional change, and as more basic research on these methods is conducted, the techniques and ideas contained herein will become outmoded." I take this to mean that if we knew more about the enzyme systems operating in physiological processes, and more about how those enzyme systems work, we could design better toxicological tests.

To quote Frawley further (p. 710): "Many tech-

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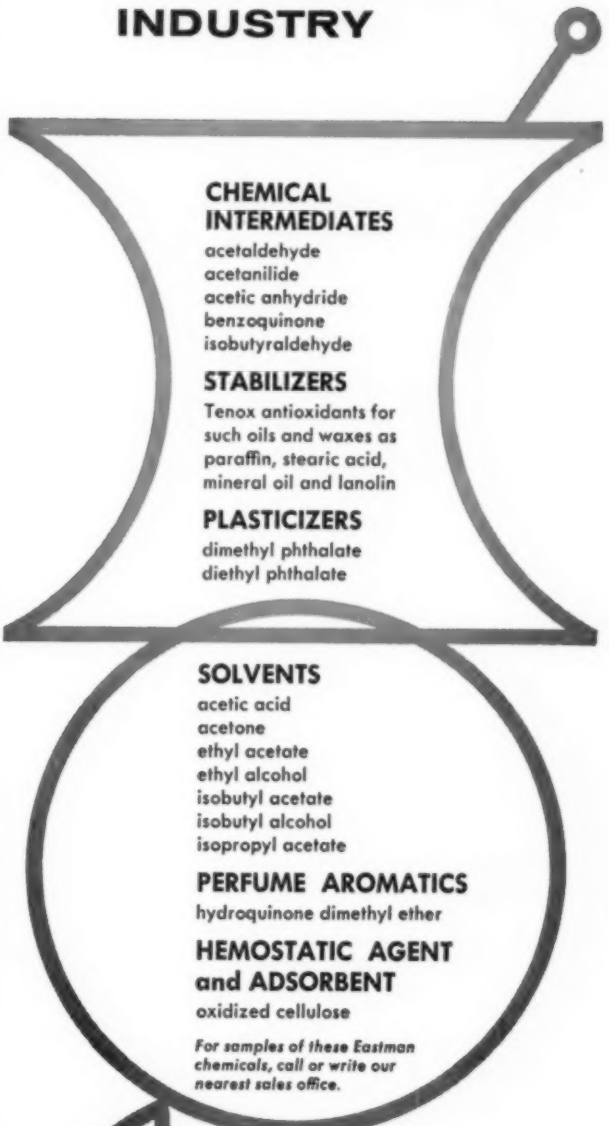

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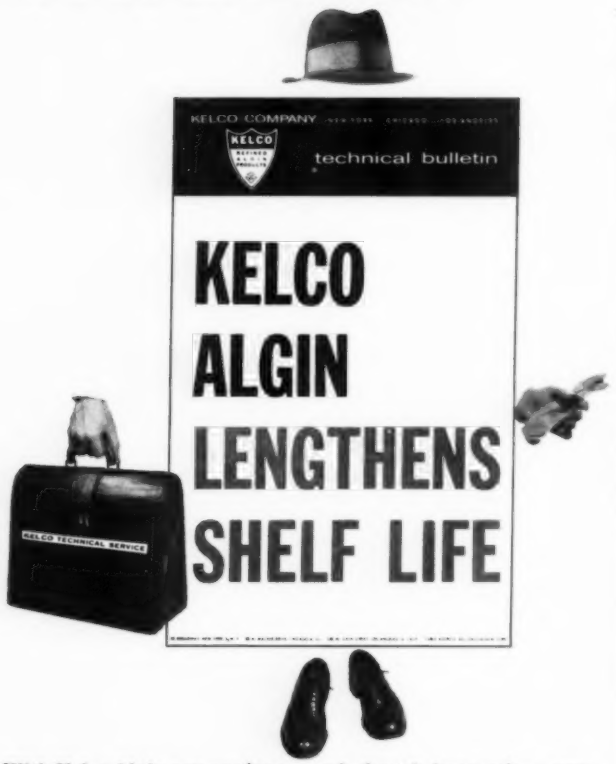

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niques have been developed for determining the effect of a compound on various biochemical systems of the body. However, it is not feasible, for example, to study the effect on every known enzyme system of the body. Screening tests must be available for studying these systems in classes and thus eliminating the majority of unaffected systems in a reasonable period of time. Unfortunately, research on such screening tests is in its infancy, and many effects will go unnoticed until they are perfected." In other words, we must understand enzyme mechanisms better before we can classify enzymes adequately, so as to devise practical tests for their sensitivity to a given chemical.

Our present incomplete knowledge of enzymes does not provide means for comprehensive testing of a substance to determine what enzymes it may interfere with. It is easy to see that fuller knowledge of enzyme structure and function would make possible:

1. Grouping of enzymes by a more adequate and significant system.
2. Prediction of a substance's effect on enzymes from its chemical structure.
3. Practical determination of the substance's behavior toward enzymes more comprehensively and systematically than is now possible.
4. Greater understanding of the physiological consequences of the above behavior.

Tests on animals will still be needed for corroboration of any conclusions as to safety drawn from such chemical tests, but many substances will be screened out by the improved battery of enzyme tests, and the animal tests will become less empirical and formidable, and more meaningful and dependable. Money spent now on basic research will pay off in savings of time and expense in future toxicity tests, aside from the greater certainty that should result.

The above is only one example of the many highly desirable results to be expected from a concerted attack upon the protein-enzyme problem. Other problems of similar importance could be cited.

Study of Basic Mechanisms Needed

A. H. Holland, Jr., Medical Director of the Food & Drug Admn, in another recent article[2], has pointed out the inherent incompleteness of biological data. "By definition almost, I think it may fairly be said that all biological data is incomplete as distinguished from inadequate data. There always remain other variables which are unknown in any biological system. This may be further emphasized by the concept that all biological systems are test systems be they subject for investigational or therapeutic purposes. At any one time a given bio-system or series of bio-systems may inexplicably fail to respond as predicted or may respond in a hypersensitive, or idiosyncratic, or other adverse fashion. At best, then, we are dealing with biostatistics in which probability must play a major role."

When the subjects of an experiment are animals,

numbered in tens, hundreds, or even thousands, statistical problems will always be present. When the subjects are molecules, numbered in the trillions, statistical problems vanish.

Holland[2] cites as specific examples of the incompleteness of the biological data obtained in extensive experimental studies, the unexpected side effects of cortisone and of the Rawolfia alkaloids, recognized only after their long-term, large-scale use by humans.

Quoting Holland further: "One cannot be but awed by the tremendous pharmacological literature in this country alone. Yet it never ceases to impress me that only a relatively small segment of it is really concerned with basic mechanisms. Only insofar as we can develop knowledge along these lines will we really be able to resolve many of the problems which now confront us."

These quotations serve to emphasize what is most needed in order to improve and expedite the development and evaluation of effective and safe new drugs and cosmetics. It is *not* further elaboration and extension of the already cumbersome pharmacological tests. What is *needed* is a concerted, intensive, and penetrating study of the *basic mechanisms* mentioned by Holland as forming so small a portion of the vast pharmacological literature. We must find out the *mechanism* of sensitization: which components of which particulates of which cells are affected by each class of sensitizers. We must find out the structure of the components involved, and study their chemical reactions so that prediction of sensitizing action on the basis of chemical structure will be possible We must fill in the gaps in our present knowledge of chemistry and chemical physics to include full understanding of secondary intermolecular forces of various types, spatial configurations, steric hindrance, etc., which are so important in the behavior of large molecules. This is a problem too big for one industry or for piecemeal attack.

Leaders of the Food & Drug Administration have shown continuous friendly interest in our industry's problems. Their scientists have contributed 15 papers to our programs, giving us valuable information on methods of improving safety and efficacy. Their laboratories have carried out many excellent studies which have assisted and guided the progress of our industry. Other Federal agencies are carrying out scientific studies on problems of wide variety, some of which shed light on protein-enzyme mechanisms. A random example is the work of Greenstein and coworkers in the National Institutes of Health which is being reported in a series[3] of papers on rotations of diastereoisomeric amino acids and a new structural rule applicable to many natural amino acids; and another series[4] on configuration of polycysteine peptides. Many excellent fundamental studies are also being carried on under federal grants in universities, research institutes and private organizations.

It appears fitting that studies such as the one cited, so fundamental that their results will open up new

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* *The Dispensatory of the United States of America, 1950 Edition*

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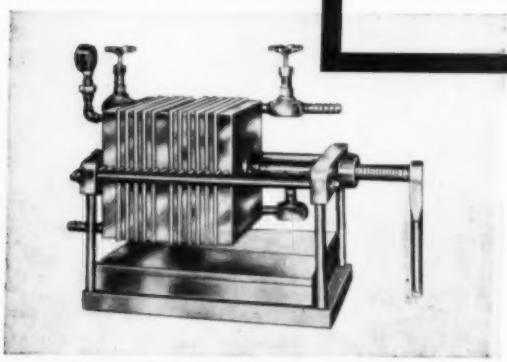

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vistas in all technologies dealing with living organisms, should be financed largely by the general populace, through the proper Federal agencies. Encouraging assistance is being given from other sources, as exemplified by Pauling's outstanding work on protein structure[6] at the California Institute of Technology, and grants of $70,000 for two studies of protein molecule structure recently made by the Rockefeller Foundation. At the fourth Henry Ford Hospital Symposium[7], held in November 1955, on the subject of enzymes as units of biological structure and function, new data and concepts were presented which added substantially to our understanding of many vital processes. Nevertheless, the central responsibility for concerted attack on such problems rests with our elected representatives. The Manhattan Project demonstrated that concentrated effort can accomplish, in a few years, the results which would require decades of random work. Surely, improvement of the public health is an objective fully as worthy as development of the atomic bomb.

President Eisenhower's proposed budget[8] calls for 2.6 billion dollars for research and development in the coming fiscal year. The Department of Health, Education, and Welfare is to be allotted 116 million dollars for research and the National Science Foundation 12 million. The Food and Drug Administration[9] is slated for an appropriation for operations of $6,779,000, an increase of 17 per cent over the current year, but a large part of the increase is earmarked for more inspectors, rather than for additional research.

The National Institutes of Health conduct research on their own premises, and make grants to outside laboratories for research projects. Among the topics mentioned in the 1954 report of the Department of Health, Education, and Welfare[10] many are of interest to the cosmetic chemist, for instance:

Protein synthesis
Contact dermatitis
Fate of cortical hormones
Effect of growth hormones on collagen production
Effect of antibiotics on dental caries
Vitamin therapy in wound healing
Drug-inactivating enzyme system
Mechanism of artery hardening
Fluorescence analysis
Microanalytical methods on single-cell level
Electrical activity patterns of cerebral cortex.

The National Science Foundation has listed[11] the extramural Federal grants and contracts for unclassified research in the life sciences made in the fiscal year 1954. The projects listed total 8,144; the cost is $64,730,900. Of the 20 categories comprising the list only one, molecular biology, contained many titles of direct interest to the cosmetic chemist.

The projects in molecular biology totalled approximately 800, and cost $7,485,000. Of these, 143 were judged to deal with topics of potential value for cosmetic chemists, such as:

Cell growth and metabolism

Effect of steric hindrance of diamines on metal binding
Chemistry of plant gums and mucilages
Metabolism of artery tissue
Interaction of antibodies and small molecules
Hypersensitive and immune states
Biosynthesis of cholesterol
Formation of connective tissue constituents, etc.

Outweighing by far all other such topics, however, were the titles dealing with protein synthesis or structure, or with enzyme mechanisms; these projects numbered 86 out of the 143 considered of value to cosmetic technology.

It is impossible to judge, on the basis of a list of titles, the depth of these projects. Some of them appear to be designed to penetrate rather deeply into the strata where enlightenment may be found.

Members of our industry should support the appropriation of adequate funds for fundamental research projects in or under support of suitable governmental agencies. They should urge these agencies to make a concerted, sustained, and penetrating attack on the basic problems which must be solved in order to improve the efficiency and effectiveness of their efforts and our own to provide better foods, drugs, and cosmetics.

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9. Anon., *Ibid* **34**, 562-564, New muscles for F.D.A.?
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PLANNING THE RESEARCH PROGRAM OF A PHARMACEUTICAL COMPANY

(Continued from page 47)

process of trial and error. Further basic study of chemico-physiological problems may lead in time to the systematic elaboration of synthetic medicinal chemicals so that a chemist can produce a new chemical compound in the confident knowledge that he is making a cure for cancer, diabetes, tuberculosis, trachoma or mental disease. That day, however, is not yet in sight.

Controlling the Research Program

This does not mean, of course, that no control can be exercised over the research program and that the individual scientists must be allowed to pursue indefinitely any field of investigation that may attract their interest. Scientists do not always apply such

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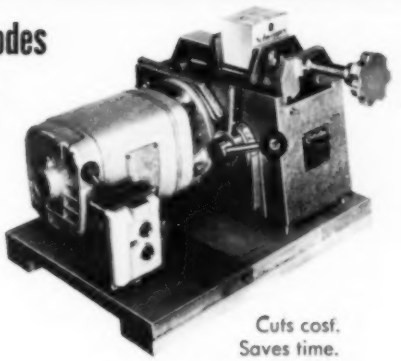

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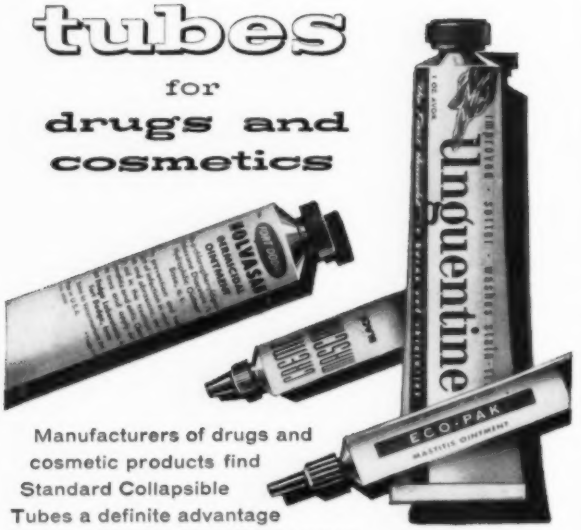

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cool and dispassionate judgment to their work as laymen sometimes imagine, and pride of authorship can be very strong indeed. There should, therefore, be close control of progress on almost every research project on a week-to-week basis to ensure immediate recognition and evaluation of new and unsuspected applications or of stumbling blocks (e.g., excessive toxicity or side reactions) as soon as they occur. To make such control effective, a breadth of knowledge from many branches of the chemical and biological sciences must be brought to bear on every problem. To make clear how this is accomplished it is necessary to explain somewhat further the organization of a typical research department in a pharmaceutical company and its relation to the company's other departments.

To simplify matters the organization adopted at CIBA will be described. It cannot differ greatly from that in other pharmaceutical companies.

The Company is divided into four departments—administration, production, research and sales—all of which are of equal standing and importance. The Research Department is headed by two vice presidents, a Vice President in Charge of Research (who obtained a Ph.D. in experimental physiology and is also a doctor of medicine) who is generally responsible for the entire Department and specifically for the biological and medical work, and a Vice President and Director of Research who is a chemist and is particularly responsible for all phases of the chemical work including developmental (pilot plant) and pharmacy research. These two vice presidents are members of the Executive Officers' Committee which, under the Board of Directors, runs the company. They thus participate, and indeed play a leading role, in making all policy decisions and have intimate knowledge of the manufacturing and sales operations.

Just as the over-all company policy is made by the Executive Officers' Committee, so the policy of the Research Department is made by a group within the Department called the Research Board. It is composed of the directors of the six divisions into which the Research Department is divided. It is these men with their varied knowledge and experience in different fields of science who, meeting every week, exercise control over the execution of the research program.

To make clear the functioning of the Research Board the six divisions in the Research Department will be described briefly. In the order in which they are normally concerned with the discovery and development of new products they are the following:

First, naturally, is the Chemical Research Division, which in turn is divided into a bio-organic and an organic chemistry section. There are a number of group leaders in each of these sections.

Next comes the Macrobiologic Research Division which is divided into sections concerned, respectively, with pharmacology, endocrinology, physiology and biochemistry.

The Microbiologic Research Division contains sec-

tions specializing in bacteriology, virology and parasitology.

The Developmental Research Division is responsible for the development of new processes and the improvement of existing processes for the chemical manufacture of the Company's products. It is this division that operates the pilot plant.

The Pharmacy Research and Development Division is responsible for the development of formulae and processes for the compounding of new products and new product forms and the improvement of formulas and processes for the compounding of existing products of the Company.

Finally comes the Clinical Research Division which is composed entirely of doctors of medicine and is responsible for all activities involved in determining the clinical, therapeutic and diagnostic effects and uses of the products developed in the research laboratories. It is obvious that the Director of the Clinical Research Division must maintain close and continual liaison with the Production and the Sales Departments, so that as the time for introduction of a product draws near these other departments may initiate the work required of them.

The section and group leaders in the Chemical, Macrobiological and Microbiological Research Divisions also meet every week to discuss the progress being made on their respective projects and the obstacles that are being encountered. Thus the work is reviewed weekly at two levels and decisions reached either to continue or increase the effort on individual projects or to drop them.

In addition to these weekly meetings at the departmental and divisional levels, the division heads and all senior members of the research staff meet three or four times a year in seminars to discuss previously designated broad scientific topics related to the Company's research program. The purpose of these meetings is the creation of closer understanding and better teamwork between all the senior members of the various research divisions. The general nature of these meetings may be gathered from the topics chosen for discussion in 1956 which include "Bacterial Resistance," "The Fate of Drugs-Tagged Molecules," "Tropical Diseases" and "New Developments in Endocrinology."

Lastly nine or ten meetings are held each year which are attended by all of the scientifically-trained members of the research staff. These meetings are addressed by outside speakers who are preeminent in various fields of science and are designed to keep the research staff informed of important advances, from basic research to applied technology, in the various fields of the Company's interests.

Thus every scientifically-trained member of the Research Department plays some part in the formulation and planning of the research program. And in order that their efforts may be coordinated, the two Vice Presidents in the Research Department have the task of making the final decisions as to the projects

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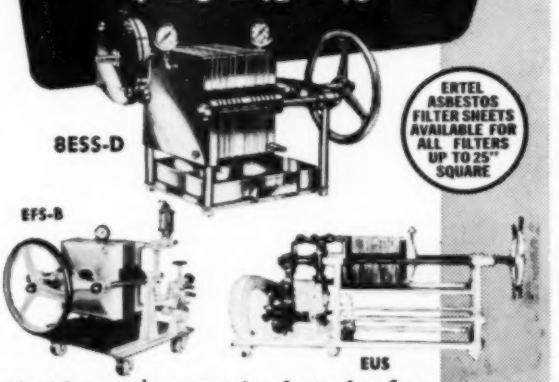

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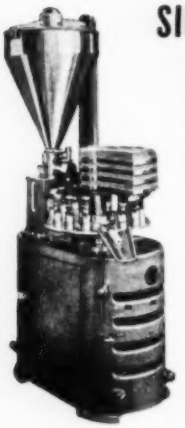

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to be undertaken, the personnel to be assigned and the relative effort to be committed. There are, finally, two respects in which these two Vice Presidents in their turn are subject to control by the Executive Officers' Committee, just as are the heads of the Administration, Production and Sales Departments. They cannot add to the personnel of their department nor can they make capital expenditures for plant or equipment without the consent of the Executive Officers' Committee. If the amounts involved for any addition are sufficiently large, the expenditure must be authorized by the Board of Directors.

These are the ways in which the required control of the research program has been assured while still preserving as much initiative as possible for the individual scientists, and assuming that the over-all size and direction of the program is kept in line with the Company's capabilities and objectives.

Conclusion

Thus CIBA's experience has shown that its research activity has been the key to the economic development of its pharmaceutical business, and that planning and coordinating this activity has been possible and beneficial. The directors and members of the top management—the men who have created the organization, brought about the large-scale application of the discoveries of the research scientists, raised the capital and shouldered all the other responsibilities and risks of running the enterprise—play the basic role in planning the research program. For by fixing how much of the Company's capital shall be invested in research facilities and how much of its income shall be devoted to the conduct of research, they determine the general scope of the research program. And because they select the top scientists who are to direct the research effort, they also determine the broad fields in which it shall be concentrated.

No flat rule has been found for determining how much of the Company's capital and income should be devoted to research. Research budgets cannot fluctuate from year to year, but must be given steady and continuous support. Experience has shown that for a pharmaceutical company the dedication of approximately one-third of its fixed assets and one-fifth of its personnel and payroll to research is about what is required to enable it to maintain its position in this very competitive industry.

The heads of the Research Department are fully familiar with all of the financial, sales and production problems facing the Company and indeed play a major role in making Company policy. The Research Department is carefully organized in divisions, each of which has its own laboratories and other essential facilities. Within the scope of this organization the top scientists in the research department leave a large measure of choice and initiative to their division heads, group leaders and other senior research workers, but they must bear the final responsibility for the individual projects to be undertaken and the relative

effort to be committed to each. Preference is given to thorough and exhaustive work in the fields selected, rather than the spreading of the research effort thinly over a wide range of subjects.

Constant control over the progress of the various projects is achieved by weekly meetings both at the departmental and divisional levels. Coordination and teamwork between the scientists in the various divisions whose collaboration is essential for the discovery of a new pharmaceutical product is also achieved through holding periodic seminars and other meetings for the exchange of information.

These are the methods by which we have found over a long period of years that group research in an industry requiring the cooperative efforts of scientists trained in a number of different disciplines can be made to produce genuinely valuable results.

SHAMPOO EVALUATION

(Continued from page 45)

Conclusions

A method of determining lathering properties of shampoos on men's heads has been presented and variations in amounts used noted. This variation can be due to the amount and type of detergent present. Relative lathering power can be determined.

Actually the residue left on hair by this test method may be removed in *in vivo* shampooing by drying with a towel or in the combing or brushing process. It is of interest, however, to note some shampoos do leave residues.

Table II
Film Residues of Various Shampoos on Dark Brown Hair

OK—No film or coating
Sl F—Slight film or coating
F—Film or coating

Stick No.	Product	Washings 1st	2nd	3rd	8th
Tap Water					
1	A	OK	OK		
1	I	Sl F	F		
1	J	OK	F		
1	K	Sl F	F		
2	C	Sl F	F		
2	A	OK	OK		
2	L	OK	OK		
2	B	Sl F	F		
3	E	OK	OK	OK	Sl F
3	M	Sl F	Sl F	F	F
3	A	OK	OK	OK	OK
3	N	OK	Sl F	F	F
4	O	OK	OK	OK	OK
4	P	OK	OK	OK	OK
4	Q	OK	OK	OK	OK
4	A	OK	OK	OK	OK
6	E	OK	OK	OK	
6	C	Sl F	F	F	
6	A	OX	OK	OK	
6	R	OK	OK	OK	
6	S	OK	OK	OK	
Distilled Water					
5	E	OK	OK	OK	
5	C	OK	Sl F	Sl F	
5	A	OK	OK	OK	
5	R	OK	OK	OK	
5	S	OK	OK	OK	

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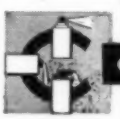

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(Continued from page 43)

sarily germicidal to bacteria and viruses, compatible with other ingredients, very mild, impart pleasant odor and taste, and have sustained activity and no deterioration.

When kissing is physically nauseating due to filthy contacts, you can bet it will be bacteriologically contra-indicated also.

The advertising slogan "kissing sweet" when applied to breath and lips is a hygienic must.

Babies should not be kissed on the lips under any circumstances by children or adults. Ask your pediatrist.

Chlorophyll has recently been incorporated in tooth pastes, mouth washes, tablets and candy. None of these preparations have any effect on the incidence of mouth or lip bacteria, but clinical investigations indicate clearly their deodorant activity.

Persons suffering from upper respiratory infections such as: colds, flu, rhinitis, virus X, sore throat or pneumonia, etc. should not be kissed on the lips.

Persons in hospital communicable disease wards should think twice before kissing once.

Our results show trends, not infallible statistical data. The evaluations and interpretations are subject to wide ranges of environmental effects.

Bacterial flora may vary from day to day, influenced by air temperature, humidity, season, climate, altitude, food intake, dush inhalation, or daily work environment.

Acknowledgment

The many human guinea pigs in this experiment who would rather kiss a blond, but who were talked into pressing their reluctant lips on sterile nutrient culture media, or blood agar base substitute.

P.S. After reading this manuscript, you will probably say "To Hell With The Kissing Bugs," and the author can only utter an understanding AMEN.

BEAUTICANS RESPOND TO PACKAGE APPEAL

(Continued from page 57)

Having decided on this step we called in the late John Stengren who designed the individual carton. The box, holding a dozen bottles, was adapted by Norbert Jay from Mr. Stengren's design after the latter's death.

Impressed by the job that The Lord Baltimore Press had done for others in the cosmetic field, we retained that organization to produce our new box. Using its famed Fidel-I-Tone fine-screen process, which reproduces color photographs on boxboard with a quality equal to that of the best slick-paper magazines, Lord Baltimore turned out a magnificent box for us, using five colors plus gold bronze. The reproduction of a photograph of a silver-haired model was indistinguishable in quality from the original print.

The handsome appearance of the package has enabled it to serve as a springboard for "Come Alive Gray." We merchandised the package almost as much as the product itself during the introductory phase, using giant blowups of the carton. The package was featured in our advertising and publicity. The black, gold, gray and white on the box blends nicely with the decor of beauty salons, too, a point considered in designing the package.

Filling a long felt need, the product has had wide acceptance ever since its introduction. The package has done much to stimulate sales.

It may well be that we have started a trend since beauticians might be thought to be interested only in contents. Nevertheless, it is our belief—which has been justified by results—that a product, whether intended for professionals or the public, should have a package that matches the quality of the product itself.

RECENT PATENTS

(Continued from page 116)

3-Hydroxy-N-Methyl-Morphinanes.

2,744,113—**Hoffmann-La Roche—1-Isonicotinyl-2-Alkenyl-2-Alkyl-Hydrazine.**

2,744,114—**Eli Lilly—Pyridoxine Synthesis.**

2,744,116—**Purdue Research Found. — Bis - (Amino-triazolyl)-Hydrocarbons.**

2,744,117—**Farmaceutici Italia—Preparation of Choline Ester of Urocanic Acid.**

2,744,118—**Parke, Davis — Phthalimidopropionylaminoethyl Disulfide.**

2,744,119—**Merck — Phthalyl - Alanyl - Mercaptoethyl Amides.**

2,744,120—**Olin Mathieson — 1 - Dehydrotestololactone.**

2,744,122—**Syntex—Δ^4 - 19 - Nor - 17α - Ethinyl-androsten-17β-Ol-3-One.**

2,744,131—**Farmaceutici Italia—Preparation of Threo - 1 - Phenyl - 1, 3 - Diacyloxy - 2 - Amino - Propane-Hydrochlorides.**

2,744,135-140—**Farmaceutici Italia—Preparation of Threo-1-P. Nitrophenyl-2-Acylamino-or 2 Amino 1, 3-Propanediols.**

2,744,137—**Hoffmann-La Roche — N - Methyl - β-Cyclohexen-(1)-Ylethylamine.**

2,744,138—**Farmaceutici Italia — Diguanidino - Phenol Ethers.**

2,744,139—**Bristol Labs. — Basic Ethers of Phenols.**

2,744,141—**Norwich Pharmacal—Prepn. of Saturated Aliphatic Beta-Secondary- and Tertiary-Amino Alcohols.**

2,744,142—**Ortho Pharmaceutical—Reduction of a Conjugated en-yne to a diene.**

2,744,851—**E. Fougera & Co.—Cardiac Glycosides fo- Intramuscular Injection.**

2,744,852—**Louis S. Goodman—Medicinal Composition Containing Diphenyl Dihydro or Tetrahydroglyoxaline-4-One and Method of Producing Anti-Convulsant Activity.**

2,744,892—**Schenley Industries — Crystallization of Dihydrostreptomycin.**

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2,744,901—**Smith, Kline & French Labs.—Bis-Tetrahydro-1-Isoquinolyl Quaternary Ammonium Salts.**

2,744,909,10—**Bristol Labs. — 2 - (Ortho - Phenyl-benzyl) and 2-(Ortho-Benzyl-benzyl) Imidazolines.**

2,744,912—**Soc. Usines Chim. Rhone-Poulenc—4-O,O-Diphenylphosphonylamino-Antipyrin.**

2,744,916—**Cutter Labs. — Phenyl - Substituted Salicylamides.**

2,744,918—**Am. Cyanamid—Substituted Phthalides.**

2,744,930—**Olin Mathieson — N,N - Diphenyl - N'-Aminoalkylene-Ureas.**

2,744,931,2—**Am. Cyanamid—Anhydrochlortetracycline.**

2,745,783—**Geigy—Substituted 1,2-Diphenyl-3,5-Dioxopyrazolidines.**

2,745,784—**Chas. Pfizer—11β, 14a, 17a, 21-Tetrahydroxyprogesterone.**

G. D. SEARLE & CO.

(Continued from page 35)

"Searle's financial history shows a consistent healthy conservatism in every period of its operation. Capitalized solely by common stock and surplus, Searle has expanded repeatedly without resort to long-term debt. The company's only external financing occurred in 1947 when short-term building loans were obtained and repaid within a year. Examination of its balance sheet reveals an extremely strong position. . . .

"Despite the vast increase in production output and the expansion of physical facilities in the past few years, there is approximately the same number of employees in production operations today as there was five or six years ago. Examples of productivity gains can be seen in almost every area of production. However, since direct labor constitutes only a small proportion of product cost, increased efficiency in chemical processes and yields have been far more important to the company.

"Production efficiency in the pharmaceutical industry is moderated by the absolute need for product quality and purity. Searle spends as much on quality control as on direct labor. The company gives its

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quality control department maximum freedom to accept or reject its products at any stage of production. The department is independent of all divisions of the company, although working closely with them. Inspectors of ampuls and tablets are actually encouraged to take whatever time is needed to assure quality, and drug lots move from one production stage to the next only after specific clearance by the control department.

"Each new product developed by research is given a gradual and carefully supervised transition from pilot stage to full production. Pilot plant operation is observed by production heads, and a pilot crew produces the first production runs before the production department takes over.

"Searle has an outstanding record of employee-management relations. Most employee matters are handled at the supervisory level or through the personnel department. However, top officers are available—and are actually called in—when employees wish to discuss problems above the supervisory level. Searle has never had a labor dispute or work stoppage for any reason. On the other hand, the company has never had a lay-off.

"Job evaluation and a merit rating system cover about 97 per cent of Searle employees. The high *esprit de corps* within the company and the satisfaction of employees with all aspects of the company have been established by the low rate of turnover of Searle employees and by confidential employee opinion polls conducted by independent opinion research organizations at management's request. Perhaps the best evidence of employee faith in the Searle management was their favorable reaction to employee stock option plans introduced in the past years. As a result of these plans, 70 per cent of Searle employees—including hourly workers—are shareholders in the company. In some departments the percentage is considerably higher. . . .

"About 85 per cent of Searle's domestic sales are made to wholesale druggists, most of the remaining 15 per cent to hospitals. The mainstays of Searle's sales effort are 300 salesmen or detail men. . . .

"Searle's sales force is headed by Franklin P. O'Brien, vice-president in charge of sales and distribution, and a director in the company. Reporting to Mr. O'Brien are the director of advertising, the director of trade relations, the director of medical service, the director of sales education, the director of sales service, and the heads of the company's two foreign sales operations. The seventeen divisions of the sales staff are controlled by the director of medical service through divisional sales managers.

"Searle's domestic distribution system consists primarily of three shipping centers located in Chicago, Lyndhurst, New Jersey, and San Francisco. These centers serve a total of 2,166 hospitals and 349 wholesale druggists. . . .

"Foreign sales have become increasingly important at Searle in recent years. At present over 13 per cent of sales are made in foreign markets. Canada and South America were the first foreign markets developed, but the company now has a subsidiary in England and operates in other countries as well, chiefly through distributorships. There is a widespread need for Searle drugs, and it is reasonable to expect that within a few years the company will materially increase the present percentage of sales derived from foreign markets.

"G. D. Searle & Co. has been fortunate that executives with the company since it was small have been able to develop at a rate commensurate with the growth of the company. These men have provided an important executive nucleus. Because of its rate of growth, however, Searle has had to go outside the company for many of the additional executives it needed in both research and sales. . . .

"John G. Searle, president, must be credited with the major role in the success of Searle. In the thirty-three years in which he has been with the company—twenty of them as chief executive—he has made the vital decisions which brought Searle into the specialty field and into its present research policies.

"Equally important for the success of the company, John Searle has selected executives with growth potential as great as the company's and then developed them fully. In many cases, as with the outstanding director of research, Dr. Raymond, this has meant the transformation of men of purely scientific background and experience into capable business executives. Although the company is guided today by a capable management team, its leadership by John G. Searle will undoubtedly spark its continued development."

DEPILATORIES

(*Continued from page 48*)

thioglycolates, the principal agent being calcium thioglycolate. In this classification lie a number of compounds all possessed of an active reducing agency and relatively non toxic. In addition, they are extremely stable to hydrolysis and are therefore relatively free from offensive odors. Though they may have an odor in conjunction with their actual use, this is relatively mild and due to degradation products of the hair rather than the thioglycolate itself.

The use of thioglycolate and many other mercaptans is covered by patents, and these should be studied if interested in the development of depilatories in which these agencies are used. Most of what follows is drawn from the patent literature.

The greatest advantage in the use of the thioglycolates lies in the ease with which they may be incorporated into an aqueous vehicle such as a cream, so that they could be used directly from the container without any previous manipulation, as is necessary with the metallic sulfides. It is therefore possible to attain a product with the cosmetic elegance free from markedly offensive odors. In formulating such a cream, the fact that the active agency is usually a calcium salt

(calcium thioglycolate) more or less eliminates the use of a soap as an emulsifying agent. This is due to the formation of an insoluble calcium soap which would precipitate and therefore break the emulsion. Since the cream must of necessity have a pH very much on the alkaline side, a further restriction must be applied to substances which are readily saponified. Glyceryl monostearate and other hydrophilic esters must therefore be eliminated from consideration. The choice is therefore narrowed to a classification of substances containing no ester linkages and which are compatible with the calcium ion.

Most of these substances are nonionic surface active agents and these are the best source of compounds for emulsifying agents in a vehicle containing the qualifications necessary for a depilatory. There are a large number from which proper substances could be drawn and now commercially available. Cetyl and stearyl alcohols could be used in conjunction with polyethoxylated alcohols. Synthetic surface reducing agents have been appearing with great frequency, so great, in fact, that it is difficult to check their possibilities in conjunction with different applications. A noteworthy example is the development of mixed polyethylene and polypropylene glycol ethers. Substances such as these fit into the category desired.

The drying time of the film after application is also an important factor, since if the water evaporates too soon the reaction will be markedly inactivated. The use of humectants is therefore highly desirable as is the introduction of fillers to prevent the too rapid evaporation of the water. The filler is also important as means of providing a visible sign of where the cream has or has not been removed after being allowed to stay on the skin for the required interval of time. Fillers, such as talc, kaolin, chalk and the hydrophilic silicates, such as the synthetic magnesium and aluminum silicates are also good fillers for such an application.

The depilatory need not be limited to use as a cream. Indeed there are several successful depilatories on the market in lotion form as well. In this case, consideration should be given to the viscosity of the emulsion formed since the applied film must be of sufficient thickness to stay moist during the interval of application and to ensure a sufficiently high concentration of the thiogylcolates in the area of depilation.

The concentration of thiogylcolate used must vary with the film thickness and drying time of the film. The patent literature discloses a concentration of about five per cent, but this figure is highly variable in practice.

The thiogylcolates have captured the major portion of the depilatory market, but still available are the old wax and rosin mixtures which remove hair completely by mechanical means. These preparations are difficult to use and, indeed, painful since they actually pull the hair out instead of destroying it chemically. These are mentioned merely to fill in the record.

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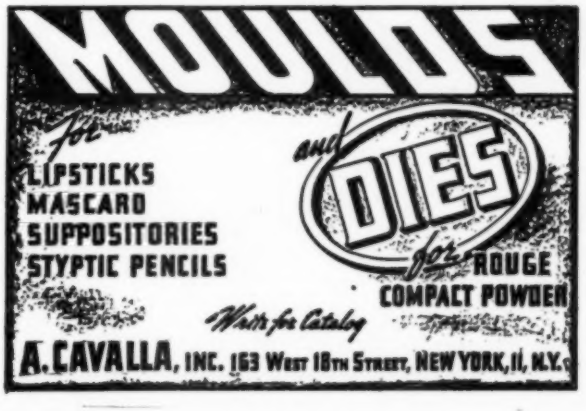

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